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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., AND NORTON (WATERFORD) LTD., PLAINTIFFS, v. CIPLA LTD., CIPLA LTD., AUROBINDO PHARMA LTD., AUROBINDO PHARMA USA, INC., and AUROLIFE PHARMA LLC, DEFENDANTS	Consolidated Civil Action No. 2:20-CV-10172-JXN-MAH **CONFIDENTIAL**

REPLY EXPERT REPORT OF GREGOR ANDERSON ON INVALIDITY

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I. INTRODUCTION

1. Counsel for Defendants Cipla Ltd. ("Cipla"), Aurobindo Pharma Ltd., Aurobindo Pharma USA, Inc., and Aurolife Pharma, LLC (collectively, "Aurobindo") (all collectively, "Defendants") have retained me to provide technical assistance in this action.

2. I understand that this litigation involves U.S. Patent Nos. 9,463,289 ("the '289 Patent"); 9,808,587 ("the '587 Patent"); 10,086,156 ("the '156 Patent"); and 10,561,808 ("the '808 Patent") (collectively, "the Asserted Patents").

3. I understand that Cipla and Aurobindo have both filed Abbreviated New Drug Applications ("ANDA") with the FDA seeking approval to market generic beclomethasone dipropionate metered aerosol, 0.04 MG/INH and 0.08 MG/INH products ("Cipla ANDA Product" and "Aurobindo ANDA Product," respectively, or "Defendants' ANDA Products").

4. I understand that Plaintiffs Teva Branded Pharmaceutical Products R&D, Inc. and Norton (Waterford) Ltd. (collectively, "Plaintiffs" or "Teva") allege that the Defendants' ANDA Products infringe claims 1-8 of the '289 Patent, claims 1-8 and 11-22 of the '589 Patent, claims 1, 9, and 11-13 of the '156 Patent, and claims 1 and 27-28 of the '808 Patent (collectively, "Asserted Claims"). Should this list change, I reserve the right to provide my opinions on any other claims that are asserted.

5. I have previously provided opinions regarding the invalidity of the Asserted Claims in my Opening Expert Report on Invalidity dated April 29, 2022. That report is incorporated herein in full. In this expert report, I have been asked to provide opinions replying to certain points raised by Dr. David Lewis in his report dated June 14, 2022 ("Lewis Rebuttal Report").

6. I am an independent expert and not a regular employee of any party or counsel to any party in this case

II. TOPICS OF OPINIONS

7. In this report, I offer opinions on the following general topics:

- Whether the Asserted Patents are anticipated.
- Whether the Asserted Patents would have been obvious.
- Whether the Asserted Patents are invalid for lack of written description, lack of enablement, and/or indefiniteness.
- Replies to opinions set forth by Dr. Lewis in his Rebuttal Expert Report.

III. QUALIFICATIONS

8. I provided opinions regarding invalidity of the Asserted Patents in my opening expert report, served April 29, 2022 ("Anderson Opening Report"). I incorporate herein sections II, IV, and V of the Anderson Opening Report, which set forth my background, qualifications, compensation, and previous testimony. My qualifications and expertise are further described in my Curriculum Vitae, a copy of which was attached as Exhibit A to the Anderson Opening Report.

IV. MATERIALS AND INFORMATION CONSIDERED

9. In preparing and rendering my opinions herein, I have relied on my education, background, knowledge, and experience, as well as the materials cited in this report and listed in Exhibit A hereto, the Anderson Opening Report dated April 29, 2022, the Supplemental Anderson Opening Report dated May 24, 2022, the Anderson Rebuttal Report dated June 14, 2022, the Anderson Secondary Considerations Report dated June 14, 2022, the Lewis Opening Report dated April 29, 2022, the Lewis Rebuttal Report dated June 14, 2022, and the Panettieri Report dated April 29, 2022.

10. The opinions set forth in this report are based on the information of which I am aware to date. I reserve the right so supplement this report should additional information become available or should Teva present new issues in response to this report.

V. APPLICABLE LEGAL STANDARDS

11. The applicable legal standards are set forth in Section VII of the Anderson Opening Report, which I incorporate herein in full.

VI. CLAIM CONSTRUCTION

12. The Anderson Opening Report sets forth the claim constructions in Section VIII.

VII. BACKGROUND OF THE RELEVANT TECHNOLOGY

13. I provided a detailed description of the background of the relevant technology in Section X of the Anderson Opening Report, which I incorporate herein. *See* Anderson Opening Report at Section X.

VIII. LEVEL OF ORDINARY SKILL IN THE ART

14. I provided my opinion on the definition of a person of ordinary skill in the art ("POSA") with respect to the Asserted Patents in the Anderson Opening Report, which I incorporate by reference herein. *See* Anderson Opening Report at Section XI.

15. I understand with respect to the Asserted Patents, Dr. Lewis applied the following definition of a POSA in his rebuttal report:

> [A person who] would have had the skills, education, and expertise of a team of individuals working together to research, develop, and manufacture an inhalation aerosol product with a dose counter. Such a team would have included individuals with master's degrees in mechanical engineering, design engineering, or related fields, with at least two years of post-graduate experience in developing inhalation aerosol products, or bachelor's degrees in similar fields of study, with a commensurate increase in their years of postgraduate experience. Such a team also would have been familiar with a variety of issues relevant to researching, developing, and manufacturing inhalation aerosol products with dose counters. The team also would have had access to an individual

> with a medical degree and experience in treating patients with inhalation aerosol devices.

Lewis Rebuttal Report at ¶ 29.

16. I disagree with this definition of a POSA to the extent that it conflicts with my own. I disagree with this definition of the POSA to the extent that it conflicts with my own. However, my opinions would not change if Dr. Lewis' definition of a POSA is adopted. Further, I have reviewed the definition of a POSA and disagree with Dr. Lewis' requirement that a POSA include a physician. Dr. Lewis does not explain the role of a physician in designing an inhaler. In my experience designing inhalers, a physician might help identify the need for an inhaler and the condition it would treat, but a physician would not design the final product, i.e., the inhaler. In my experience, the final product would be designed by an engineer or scientist. At most, the physician will then verify and validate the needs that the physician identified.

17. It is my opinion that I satisfy both the definition of a POSA set forth by myself and by Dr. Lewis.

IX. SUMMARY OF THE ASSERTED PATENTS

18. The Anderson Opening Report sets forth a summary of the Asserted Patents, which I incorporate in full herein. *See* Anderson Opening Report at Section VII.

X. SUMMARY OF THE ACCUSED PRODUCTS

19. The Anderson Opening Report sets forth a summary of the Accused Products, which I incorporate in full herein. *See* Anderson Opening Report at Section VIII.

20. In Section VIII of the Anderson Opening Report, I explained my opinion that the Accused Products utilize the dose counter disclosed in WO 2007/124406 (the "'406 Publication"). Dr. Lewis does not rebut these opinions. Accordingly, Dr. Lewis effectively concedes that Defendants' ANDA Products are practicing a design described in the prior art.

Accordingly, to the extent that Defendants' ANDA Products do not materially differ from the '406 Publication (and they do not), the '406 Publication necessarily anticipates the Asserted Claims as I explained in the Anderson Opening Report.

XI. RESPONSE TO DR. LEWIS' SUMMARY OF THE PRIOR ART

21. In Section IV of the Lewis Rebuttal Report, Dr. Lewis discusses numerous prior art references that were referenced in the Anderson Opening Report. My discussion of these references was set forth in the Anderson Opening Report, including in Sections XIV, XV, XVI, and XVII, which I incorporate herein by reference. To the extent my discussion conflicts with Dr. Lewis's, I disagree with his opinions.

22. Much of Dr. Lewis's discussion in Section IV of the Lewis Rebuttal Report has very little to do with the grounds for invalidity of the Asserted Claims set forth in the Anderson Opening Report. As such, I have addressed his opinions, where applicable in the specific sections below.

XII. RESPONSE TO SECTION V OF THE LEWIS REBUTTAL REPORT

23. In Section V of the Lewis Rebuttal Report, Dr. Lewis purports to rebut certain alleged general assertions regarding the prior art and the motivation to combine references set forth in Sections X and XIV of the Anderson Opening Report. I respond generally to his points in this section.

24. As set forth in the Anderson Opening Report, the use of support rails otherwise known as ribs is ubiquitous in the prior art. *E.g.*, Anderson Opening Report at ¶ 169. The fact that Dr. Lewis identified a handful of MDIs in Exhibit B to the Lewis Rebuttal Report that lack support rails does not undermine my opinions. As shown by the prior art cited in the Anderson Opening Report, the use of rails, including multi-step rails, was well-known by the priority date of the Asserted Patents. As explained in the Anderson Opening Report, Dr. Lewis himself

acknowledged that the ribs were well-known before the priority date of the Asserted Patents, and described one of their functions. Lewis 2007 at 236 (CIPLA-BDA_0184749). As explained more specifically in Section XV of the Anderson Opening Report, the claimed support ribs were well-known too and a POSA would have been motivated to implement them.

25. Dr. Lewis's opinions that dose counters were not ubiquitous in the prior art misses the point entirely. Lewis Rebuttal Report at ¶ 186. Here again, Dr. Lewis points to the fact that some prior art MDIs did not include dose counters. *Id.* But Dr. Lewis ignores that dose counters were well-known long before the priority date of the Asserted Patents. Indeed, they were so well-known that the FDA effectively mandated their inclusion in MDI's through its 2003 Guidance. Dr. Lewis's focus on commercial devices ignores the litany of literature cited throughout the Anderson Opening Report discussing dose counters and their inclusion in MDIs prior to the priority date of the Asserted Patents.

26. Dr. Lewis also attempts to make a mountain out of the modifications that may be needed to adapt an existing dose counter to a particular inhaler body or canister valve. *See* Lewis Rebuttal Report at ¶¶ 190-192. Though certain changes may, in some cases, be necessary, these changes are of the kind ordinarily performed by POSAs and involve nothing more than routine skill and experimentation. Indeed, this type of engineering is highly predictable and presents a finite number of solutions.

[redacted]

[redacted] Stuart 2013 is not to the contrary. Rather, Stuart 2013 describes challenges associated with designing a dose counter from the ground up (i.e., starting from scratch). Most of those considerations are irrelevant to the grounds of invalidity set forth in the Anderson Opening Report because those grounds for invalidity start from known dose counter designs as opposed to designing a dose counter from scratch.

28. Dr. Lewis asserts that I opined that "any dose counter could be combined with any canister or any valve stem or any canister housing." Lewis Rebuttal Report at ¶ 192. Notably, he does not cite the Anderson Opening Report for this proposition. That is because I did not make such an assertion. Rather, I opined that a POSA would be motivated to combine specific features of specific dose counters and/or inhaler bodies as discussed throughout the Anderson Opening Report and below.

XIII. INVALIDITY OF THE COMMON PLANE PATENTS

A. Anticipation of the Common Plane Patents

1. Anticipation of the '289 Patent by the '406 Publication

29. Mr. Lewis' primary criticism of my analysis of the '406 Publication is an assertion that I mixed and matched embodiments. Lewis Rebuttal Report at ¶ 203. This is simply incorrect and Dr. Lewis does not identify a single instance of such "mixing and matching" in connection with my analysis of whether the '406 Publications anticipates the '289 Patent.

30. Dr. Lewis has not disputed my opinion that Defendants' ANDA Products practice the third embodiment of the '406 Publication.

a. Claim 1

31. Dr. Lewis asserts that the '406 Publication does not disclose an inner wall canister support formation. As I explained in my opening report, this is incorrect. Further, Dr. Lewis's analysis is myopically focused on the structure of the legs in Figure 28. He ignores that the '406 Publication states that the legs "mate with interior surface of the actuator housing 68 for the aerosol container 70." '406 Publication at [0119].

32. Further, Dr. Lewis ignores that the presence of an interior extending rib on the inner wall of the inhaler body will necessarily reduce rocking of the medicament canister versus the same inhaler body with no ribs. This is because an inwardly extending rib reduces the amount of space by which the canister can move. As interpreted by Dr. Lewis in his infringement report, any such rib is the claimed canister support formation, regardless of whether the canister could ever rock to the point where it could cause a count.

33. In Paragraphs 212 to 213 of the Lewis Rebuttal Report, Dr. Lewis misunderstands my point that the location of the legs in the '406 Publication evidences the location of an inner wall canister support formation. As I have explained previously, the legs or wings of the '406 Publication are explicitly described as mating with an interior surface of the inhaler body. '406 Publication at [0100], [0119]. A smooth interior surface of an inhaler body would have nothing for the legs or wings to mate to. Thus, there must be some structure in line with the legs/wings. That structure would be the claimed inner wall canister support formation. As my annotations to Figure 28 of the '406 Publication in Paragraph 124 of the Anderson Opening Report show, the legs are in a common plane with a castellation and the central outlet port. It therefore follows that the structure the legs mate with will also be in that same plane. Otherwise, the legs would not mate with that structure.

b. Claims 2 and 3 of the '289 Patent

34. Dr. Lewis does not dispute my analysis that the '406 Publication anticipates Claims 2 and 3 other than to the extent he disputes my analysis of Claim 1.

2. Anticipation of the '587 Patent by the '406 Publication

35. As I explained in the Anderson Opening Report, there is no substantive difference between Claims 1 and 12 of the '587 Patent, and Claim 1 of the '289 Patent. Dr. Lewis attempts to make it sound like one exists by referencing functional purpose language in the claims of the '587 Patent. But, as I explained in Paragraph 131 of the Anderson Opening Report, the functional purpose language in Claims 1 and 12 of the '587 Patent was entitled to no patentable weight and failed to distinguish those claims from Claim 1 of the '289 Patent.

36. Dr. Lewis also includes images of a GlaxoSmithKline ("GSK") inhaler body. However, Dr. Lewis ignores that this inhaler body plainly has no dose counter within it, and never could have a dose counter given that there is no viewing window for the number of doses remaining. Thus, Dr. Lewis' analysis of the GSK inhaler body is irrelevant to the analysis of invalidity of the Common Plane Patents.

3. Anticipation of the '289 and '587 Patents by the '514 Publication

37. Dr. Lewis makes multiple criticisms of my analysis of anticipation of these patents by the '514 Publication, each of which lacks merit.

38. First, Dr. Lewis asserts that some inhaler bodies do not appear to contain support rails, while others do. Lewis Rebuttal Report at ¶ 240. But the fact that the '514 Publication discloses inhaler bodies with support rails is what is material for my analysis. This criticism fails to address the substance of my opinions.

39. Dr. Lewis next asserts that my opinions are deficient because the '514 Publication discloses both dose counters and dose indicators. Lewis Rebuttal Report at ¶ 240. This criticism

makes little sense. As I explained in the Anderson Opening Report, the '514 Publication discloses a dose counter having the features claimed in the Common Plane Patents. The fact that it also discloses a dose indicator does not change this.

40. Dr. Lewis also criticizes me for allegedly mixing embodiments, particularly those with dose counters and dose indicators. Lewis Rebuttal Report at ¶¶ 240-41. This is inaccurate, and regardless a POSA would understand how to implement the inhaler bodies disclosed in the '514 Publication with the dose counter in the '514 Publication.

41. Next, Dr. Lewis takes issue with the reference numeral labeling in the figures in the '514 Publication. Lewis Rebuttal Report at ¶¶ 243-245. I addressed this issue in my opening report. As I explained there, a POSA reading the text of the '514 Publication would be able to understand the reference numerals in the figures, and more importantly would understand what features in the figures are being described in the text. Any errors in the reference labels on the figures are irrelevant to my analysis.

42. Dr. Lewis spends several pages asserting that the '514 Publication does not disclose the claimed actuation member under either construction. However, Dr. Lewis ignores that given the breadth that Plaintiffs contend that the asserted claims cover under their infringement theories, such interpretations would encompass the structures disclosed in the '514 Publication. From this analysis, Dr. Lewis concludes that several other limitations of the Common Plane Patents are not satisfied by the '514 Publication. This analysis is flawed for the same reason.

43. Finally, Dr. Lewis asserts that Figure 8a of the '514 Publication does not disclose an inner wall canister support formation because the structure I identified as the claimed inner wall canister support formation extends from the bottom of the inhaler body. Lewis Rebuttal

Report at ¶ 259. However, this opinion is entirely contradictory to Dr. Lewis' infringement analysis. Multiple of the alleged inner wall canister support formations in Defendants' ANDA Products extend from the base of the inhaler body. Dr. Lewis cannot interpret a patent differently for infringement and invalidity.

B. Obviousness of the Common Plane Patents

44. Dr. Lewis provides some general criticisms of my obviousness analyses on the Common Plane Patents that I address generally first. For example, Dr. Lewis opines that a POSA would have designed a dose indicator, not a dose counter. Lewis Rebuttal Report, 303. According to Dr. Lewis, this makes my analyses deficient because a POSA would never have looked to a dose counter. This simply ignores the disclosure of the prior art that I rely upon, which discloses dose counters. Dr. Lewis' theory also presumes that a POSA is designing a brand-new device from scratch with no knowledge of prior art designs. That is not the case in my obviousness opinions, and as explained above is the wrong analysis. His opinions in Paragraphs 303 and 304 depend from that incorrect starting point that ignores the disclosure of the prior art upon which I relied, which includes dose counters.

45. Dr. Lewis' opinions in Paragraphs 305, 306, and 308 to 310 of the Lewis Rebuttal Report are similar. There, he opines that a POSA would have needed to decide where to locate the dose counter, and that a POSA would have put the dose counter on the top of the device instead of integrating it. Again, this presumes that the POSA is designing a device from scratch. The prior art relied upon in the Anderson Opening Report has already made the decision of where to locate a dose counter (often in the base of the inhaler body), and notably none of my obviousness analyses change that location. Dr. Lewis is simply fighting the disclosures of the prior art.

46. Finally, I have already discussed the flaws in Dr. Lewis' analysis of Paragraph 307 above and will not repeat them in full for brevity. Simply put, the alteration of some dimensions of a dose counter, valve stem block, or inhaler body amounts to nothing more than routine engineering that a POSA would have completed without issue. It is not nearly as complicated as Dr. Lewis attempts to make it sound.

47. These flaws pervade Dr. Lewis' commentary on my obviousness analyses. I do not readdress them in each individual section.

1. Obviousness of the '289 Patent Over the '406 Publication

48. As explained in the Anderson Opening Report, the '406 Publication in view of the knowledge of a POSA renders obvious the claims of the '289 Patent.

49. As a preliminary matter, Dr. Lewis opines that a "POSA would [not] have had reason to select the dose counter of … the '406 Publication." First, this is the wrong analysis. A POSA is deemed to have knowledge of the prior art, including the '406 Publication, and Dr. Lewis does not contest that the '406 Publication is analogous art. Second, 3M, the applicant for the '406 Publication, was a leader in design and development of inhalation devices and dose counters. As early as Spring 2008, 3M was advertising its "dose-by-dose counter," reflected in the '406 Publication. *See* Exhibit B. Although Dulera was ultimately approved after the earliest priority date of the '289 Patent, the 3M dose counter was incorporated into Dulera well before that date, indicating that POSAs would select the '406 Publication, and particularly the third embodiment for development. *See* CIPLA-BDI_0004047 and CIPLA-BDI_0004646-53.

a. Claim 1

50. Dr. Lewis' primary criticism of my obviousness analysis on this claim is the alleged lack of support ribs in the '406 Publication.

51. However, Dr. Lewis has not, and cannot, contest that support ribs were known in the prior art. He disputes how ubiquitous they were in commercial products, but he cannot dispute that they were known to POSAs. He further has not, and cannot, dispute his own prior statement that years before the priority date of the Asserted Patents it was known to "introduce[] four equally spaced ribs to locate the counter and provide an annular passageway to draw air using the mouthpiece." Lewis Rebuttal Report at ¶ 236. Furthermore, Dr. Lewis himself, in a prior art publication, identified that the ribs helped to prevent accidental opening of the valve. *Id.* As Dr. Lewis seems to recognize in his analysis of the GSK device, accidental valve opening can occur from rocking. Thus, Dr. Lewis appears to have himself recognized that ribs assist with undesired actuation prior to the priority date of the Common Plane Patents. The fact of the matter is that support ribs were well-known before the priority date of the Common Plane Patents and there were known reasons to provide such ribs in an inhaler body, as explained throughout the Anderson Opening Report. *E.g.*, Anderson Opening Report at ¶¶ 169-170.

52. Putting the dose counter of the '406 Publication into an inhaler body that included ribs would have been a matter of simple engineering. As the '406 Publication explained, "[T]he dose counter 2 is designed to be usable with a variety of metering valve designs, and to fit compactly within commercially available actuator housing profiles so that it is not necessary to change the external configuration of those actuator housings to accommodate the inventive dose counter 2 therein." '406 Publication at [00105]; [00124] and [00151]. As I explained elsewhere, it is necessary to include a structure in the inhaler body to secure the dose counter of the '406 Publication, and one obvious choice for such a structure in view of the disclosure of the prior art is a rib. Such ribs would be the claimed canister support formation for the reasons I have already explained herein and in the Anderson Opening Report.

53. As explained with regard to anticipation, under Plaintiffs' infringement theories, any rib placed in the inhaler body will be in a common plane with the indexer and the central outlet port. Accordingly, that limitation would be satisfied.

b. Claims 2 and 3

54. Dr. Lewis does not address any additional issues with my analysis of these claims beyond those addressed in Claim 1.

c. Claim 4

55. Dr. Lewis further asserts that a POSA would not have used a "support rail which extends longitudinally along an inside surface of the main body." Lewis Rebuttal Report at ¶ 326. This criticism is absurd. I provided numerous examples of such ribs in the prior art. *See, e.g.*, Anderson Opening Report at ¶ 170. As a matter of manufacturing, a longitudinal rib is the easiest to manufacture in a molded inhaler body. This keeps costs down and would have been the obvious choice for a POSA.

d. Claim 5

56. As I explained in the Anderson Opening Report, based on Dr. Lewis's infringement theories, a step can include the top of the rib. Every rib therefore includes a step, and I provided numerous examples of such ribs. Anderson Opening Report at ¶ 176. Thus, Dr. Lewis's opinions on this claim are incorrect.

e. Claims 6 and 7

57. Dr. Lewis asserts that including multiple ribs would be a "more dramatic change" to the inhaler body. Lewis Rebuttal Report at ¶ 329. This criticism lacks merit. I provided numerous examples of inhaler bodies that include multiple ribs. Anderson Opening Report at ¶ 176. Such structures were known, as were their benefits. Accordingly, Dr. Lewis's opinions lack merit.

58. I also provided multiple examples of known inhaler bodies containing ribs on opposite ends of the inhaler. Dr. Lewis' opinion that these represent a "dramatic change" is unsupported. A POSA would have understood the benefits of such an arrangement (e.g., aligning a canister within an inhaler body) and how to implement these ribs as explained in the Anderson Opening Report.

f. Claim 8

59. Dr. Lewis does not meaningfully dispute my statement that "Plaintiffs have interpreted step to include both the top of a support rail, and the bottom." Anderson Opening Report at ¶ 179. Instead, he asserts that some support rails may go all the way to the base of the inhaler and thus not include a step on the bottom. Lewis Rebuttal Report at ¶ 333. This hypothetical ignores the prior art, which plainly discloses support rails that do not go all the way to the base of the inhaler. *See* Anderson Opening Report at ¶ 176. Furthermore, it ignores the structure of inhalers, which have a mouthpiece on the front. Any rib on the front surface of the inhaler cannot extend all the way to the bottom because the opening for the mouthpiece is in that location. Thus, the rib would just end where the opening begins, and under Plaintiffs' infringement theories, would have a second step.

2. Obviousness of the '587 Patent Over the '406 Publication

60. Dr. Lewis' criticisms of my opinions on the obviousness of the '587 Patent mirror his criticisms addressed above with regarding to anticipation and obviousness of the '289 Patent in view of the '406 Publication. I incorporate my prior analyses in full.

3. Obviousness of the '289 Patent in view of the '514 Publication in Combination with the '406 Publication

a. Claim 1

61. Dr. Lewis rehashes his assertion that the dose counter of the '406 Publication would not be compatible with the inhaler body of any other prior art. Lewis Rebuttal Report at ¶¶ 389-391. As I have previously explained, this assertion lacks merit. It would have been a matter of routine and simple engineering to make any modifications needed. The '406 Publication expressly states that its dose counter is compatible with other inhaler bodies. '406 Publication at [00105]; [00124] and [00151]. Furthermore, the '514 Publication indicates that minimal changes to a conventional inhaler body were required to incorporate a dose counter. '514 Publication at 25:4-12.

62. Dr. Lewis asserts in Paragraph 390 of the Lewis Rebuttal Report that a POSA would not have combined the dose counter of the '406 Publication with the inhaler body of the '514 Publication because it would not stabilize the canister. I disagree. Most canister stabilization is accomplished through the inhaler body itself. As shown, for example, in Figure 8a of the '514 Publication, the canister has a close fit with the inhaler body that would address Dr. Lewis's concern about stabilization.

63. Dr. Lewis's comments about the "actuation pin" of the '514 Publication being incompatible with the '406 Publication's dose counter pretends that a POSA is an automaton. *See* Lewis Rebuttal Report at ¶ 392. Rather a POSA would have recognized that an "actuation pin" from the '514 Publication's dose counter is simply unnecessary when using the '514 Publication's inhaler body with the '406 Publication's dose counter.

64. Finally, Dr. Lewis asserts that my proposed combination does not result in the claimed invention because "the POSA would have had no reason to select an alignment that

satisfies the Common Plane Limitation." Lewis Rebuttal Report at ¶ 393. I disagree for multiple reasons. First, there are a finite number of locations on the interior of the canister on which to place a support rib. These are all predictable and Dr. Lewis' own publication explained the reason to place support ribs around the canister. Second, as previously explained, under Dr. Lewis' infringement theories, virtually any rib will be in a common plane with the indexer of the '406 Publication.

b. Claims 2 through 8

65. Dr. Lewis incorporates his previous analyses with regard to the '514 Publication and the '406 Publication in these sections. He does not add any further analysis. Accordingly, I incorporate my prior rebuttals to his positions as set forth above.

4. Obviousness of the '587 Patent in view of the '514 Publication in Combination with the '406 Publication

66. Dr. Lewis' criticisms of my opinions on the obviousness of the '587 Patent mirror his criticisms addressed above with regard to anticipation and obviousness of the '289 Patent in view of the '514 Publication in combination '406 Publication. I incorporate my prior analyses in full. I further incorporate my prior analyses individually regarding the '406 Publication and the '514 Publication.

5. Obviousness of the '289 Patent in view of the '021 Publication

a. Claim 1

67. Dr. Lewis repeats his assertions that a POSA would not have selected the '021 Publication or one of the particular dose counters described therein. Lewis Rebuttal Report at ¶¶ 454-55. I have addressed these issues above both generally and with regard to the '406 Publication, and incorporate that analysis by reference herein.

68. Dr. Lewis also repeats his assertion that a POSA would not have recognized the benefits of support ribs because some publications do not illustrate support ribs. Lewis Rebuttal Report at ¶ 456. As I have previously explained, support ribs had been well known for many years, and Dr. Lewis explained previously why a POSA would use these ribs. Accordingly, these positions lack merit for the same reasons I have previously described.

69. Dr. Lewis also opines that it would not have been obvious to add ribs to the inhaler body of the '021 Publication. Lewis Rebuttal Report at ¶¶ 457-59. Yet, in this same paragraph he expresses concerns about the snugness of the fit between the canister and the inhaler body. *Id.* As Dr. Lewis recognized in his prior art paper, this snug fit and airflow concerns are one reason why a POSA would have added ribs to an inhaler body. Rather than impeding airflow, ribs would keep the canister spaced from the wall of the inhaler body, ensuring consistent airflow patterns. As I have previously explained, these modifications would be routine engineering and well within the skill of a POSA.

70. Dr. Lewis also raises certain other criticisms such as testing, and new molding. Lewis Rebuttal Report at ¶ 461. These are routine matters that are well within the skill of a POSA and do not impact the obviousness of the claims of the Common Plane Patents. Dr. Lewis is incorrectly approaching the obviousness analysis as if a POSA is looking to modify an existing commercial design, and approaching the obviousness analysis like a business executive who is trying to cut costs.

71. Dr. Lewis also asserts that locating a rib adjacent to the actuation member would not satisfy the Common Plane Limitation. This is incorrect. As explained in the Anderson Opening Report, the '021 Publication's actuation member lies in a common plane with the central outlet port. Placing a rib adjacent to the actuation member on the inner wall of the

inhaler body will lie in that same plane, thereby satisfying the Common Plane Limitation. Further, Dr. Lewis again ignores that there are a finite number of locations in which to place a rib on the interior of an inhaler body.

72. Finally, Dr. Lewis asserts that the experiences of the inventors of the ’289 Patent support his position. This is truly hindsight, which I understand is impermissible. Regardless, the inventors of the ’289 Patent addressed a particular dose counter (Teva’s) and reached obvious solutions that were already known in the prior art. The fact that it may have taken them a significant amount of work to do so does not make their alleged invention any less obvious in view of the prior art.

b. Claims 2 through 8

73. Dr. Lewis does not conduct any further analysis for these claims. Instead, he repeats commentary from regarding these claims from his analysis of the ’406 Publication and ’514 Publication, which I have already addressed above. I incorporate my prior analysis on these claims herein, which applies with equal weight to the ’021 Publication.

6. Obviousness of the ’587 Patent in view of the ’021 Publication

74. Dr. Lewis’s criticisms of my opinions on the obviousness of the ’587 Patent mirror his criticisms addressed above with regarding to anticipation and obviousness of the ’289 Patent in view of the ’021 Publication. I incorporate my prior analyses in full. I further incorporate my prior analyses individually regarding the ’406 Publication and the ’514 Publication as applicable.

XIV. INVALIDITY OF THE ’156 PATENT

A. Claims 1, 9, and 11-13 are Anticipated by the ’021 Publication

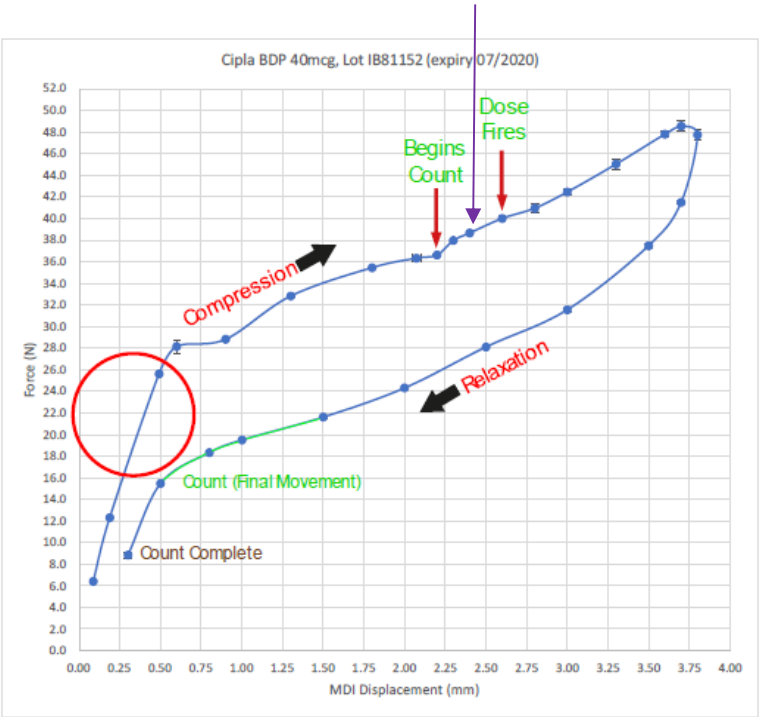
75. As an initial matter, I disagree with Dr. Lewis’s characterization of my opinion as relying on “disparate descriptions and figures in the ’021 Publication.” Lewis Rebuttal Report at

¶ 601. To the contrary, I rely on the entirety of the '021 Publication, and the aspects of the invention described therein that are consistent throughout the various disclosed embodiments. In my opinion, a POSA would recognize these similarities between embodiments and would rely on the entirety of the publication, as I have done. The mere fact that a POSA can configure the invention in a variety of shapes and sizes does not change the overarching disclosures of the publication. Moreover, while Dr. Lewis criticizes my use of the entire publication, he does not point to a particular figure that does not anticipate the claims, rather he just highlights that the publication includes multiple embodiments of the invention, as most patent publications do.

1. Claim 1

76. I disagree with Dr. Lewis's contention that the '021 Publication does not disclose firing before counting. For example, the '021 Publication explains that the actuator member in Figures 40 and 41 operates similarly to the actuator member and ratchet gear in Figures 6-9. *See* '021 Publication at [0104]. Paragraphs [0088] and [0089] describe this function, making it clear that the '021 Publication describes counting before firing, as Dr. Lewis broadly understands it.

77. Dr. Lewis has opined that Defendants' ANDA Product reaches a fire configuration ***before*** a count configuration because the count is completed on the return, ***temporally after*** firing, but ***locationally before*** the firing configuration. This can be seen in the below chart, prepared by Dr. Lewis:



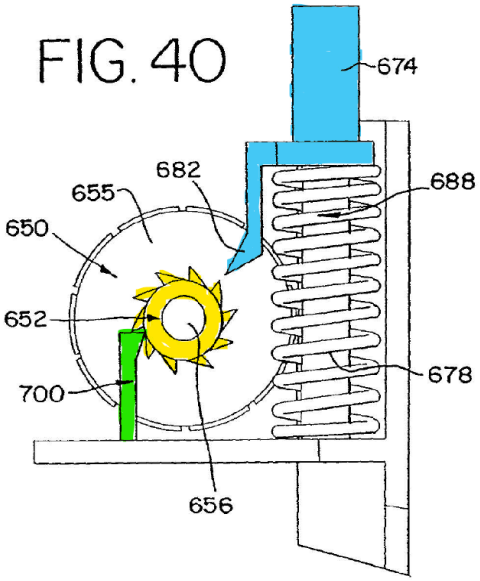
See Lewis Opening Report at ¶ 122. Notably, in Defendants' devices, if the compression is aborted before firing, but after the count begins or commits, as shown by the purple arrow above, the count will occur without firing (e.g., before firing) during "relaxation." Thus, under Dr. Lewis's interpretation, the only way for the "count configuration" to fall outside of the claim, is if the entire count begins, and is completed, on the compression stroke, before firing. That is not how the '021 Publication describes the firing sequence of its various embodiments to function.

78. The '021 publication discloses split counting, like Defendants' devices, where the count is completed on the return or "relaxation" stroke. For example, Paragraph [0088] explains that "when the container is released by the user, the spring (not shown) within the counter biases the container upwardly . . . such that the valve stem is moved to the closed position . . . ." '021 Publication at [0088]. This teaches that firing has already occurred. The paragraph continues to explain that, "as the container moves upward," the "resilient arm member" (e.g., the count pawl) is biased outwards, while the hook member (e.g., the actuator pawl) slides against a surface of

the ratchet wheel teeth. *Id*. When the container reaches the top of the stroke, the resilient arm and hook member jump over the ratchet teeth, which would complete the rotation and therefore complete the count, after firing. *Id*. Similarly, Paragraph [0089] describes a reversal of the operation, whereby "as the container moves upwardly . . . the hook member engages with the engagement surface of one of the teeth and thereby rotates the ratchet wheel an incremental amount," thus also counting after firing.

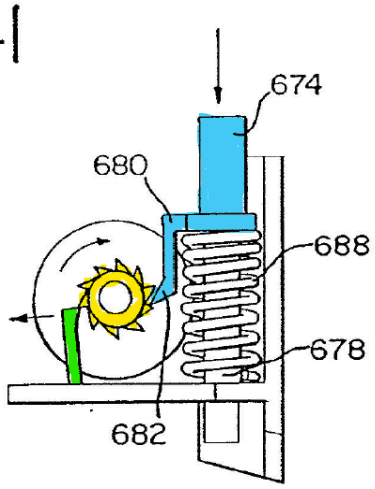
79. Dr. Lewis's rebuttal opinions rely on a misunderstanding of the disclosure of the '021 Publication and Figures 40 and 41. He contends that the '021 Publication does not support my understanding that Figure 41 is in the canister fire configuration, and repeats his incorrect assumption that the '021 Publication does not disclose firing before counting. Lewis Rebuttal Report at ¶¶ 607-608. He is wrong. As discussed above, the '021 Publication describes that firing occurs before a count is completed, that is before the resilient arm jumps over the tooth. *See* '021 Publication at [0088]-[0089]. In addition, the '021 Publication teaches that Figures 40 and 41 depict embodiments that function in the same way as the embodiments in Figures 6-9, described at Paragraph [0088]. *Id*. at [00104]. Looking at Figure 40, it is apparent that the firing sequence has not yet begun: the spring is not yet compressed, the actuation member is not yet contacting the ratchet wheel, and the image is devoid of arrows indicating movement. *See also id*. at [0063].

FIG. 40



80. Figure 41, to the contrary shows a compressed spring, an indicator member biasing outwardly, and the arrows indicating movement has occurred. *See also id*. at [0064].

FIG. 41



81. As the resilient arm depicted in Figure 41 has biased outwardly, but not yet jumped over the tooth, it is apparent that the count (rotation of indicator member 650) has not yet been completed. *See* '021 Publication at [0088]. The outward biasing of the resilient arm, however, indicates firing has occurred. *See id*. Thus, based on the entirety of information

presented by the '021 Publication, I can reasonably conclude that Figure 41 is showing the fire configuration, or at a minimum, a moment in time between the firing and count configurations.

82. Next, I disagree with Dr. Lewis's opinion that the actuator pawl disclosed in the '021 Publication is not below the datum plane in the canister fire configuration.

83. As a preliminary matter, Dr. Lewis's opinion that a POSA would be unable to locate the datum plane in Figures 12 and 7 is simply incorrect. Figure 12 clearly depicts the interior of the valve stem block 16 with upper surface 17 and well 18. *See* '021 Publication at [0075], [0085]. These same stem block parts appear in multiple embodiments. *See id*. at Figs. 5-7, 12, and 24. In addition, the '021 Publication explains that the indicator module in all embodiments, is disposed around the support block 16. *Id*. at [0108]. As explained in my opening report, a POSA would have understood that the relevant datum plane in an inhaler is the point at which the medicament is fired (e.g., where the valve stem sits on a shelf in the stem block as far as it can be inserted with an interference/sealing fit, just above the orifice of the stem block). *See* Anderson Opening Report at ¶ 371. This fit ensures an effective seal and prevents the canister from falling out—it is a feature seen on all MDIs. It is from this reference plane/point that the valve will typically open at a known distance when the canister is pushed down this minimum distance and the valve opens and allows fluid (propellant and medication) to exit. *Id*. Thus, this is the datum from which a POSA would perform calculations to determine stem length, stroke length, and other distances or lengths relevant to structuring the device. Figure 12 depicts a datum plane that, based on the knowledge of the POSA, would be determined to sit just above the orifice, where the valve stem sits and fires (shown in red). In addition, I have drawn the datum plane line at "a shoulder of a valve stem block" (shown in blue) and the location is the same.

FIG. 12

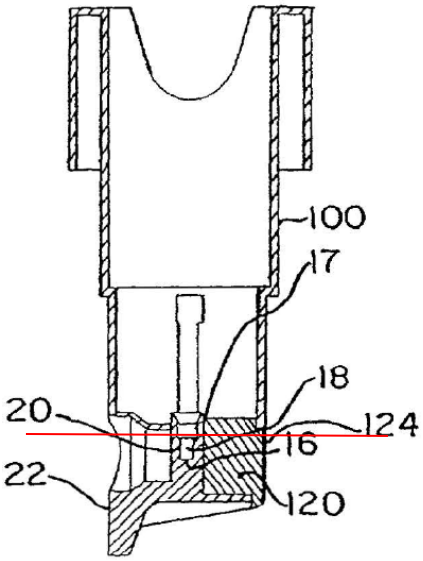
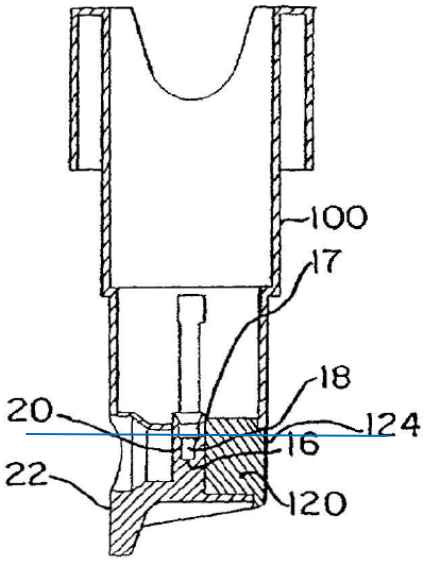


FIG. 12



Contrary to Dr. Lewis's opinion, a "shoulder" is plainly visible (red arrow), and nearly identical in appearance to the shoulder identified in Figure 9 of the '156 Patent (falling just above the nozzle/orifice 20 in Figure 12 and well/sump in both Figures):

FIG. 12

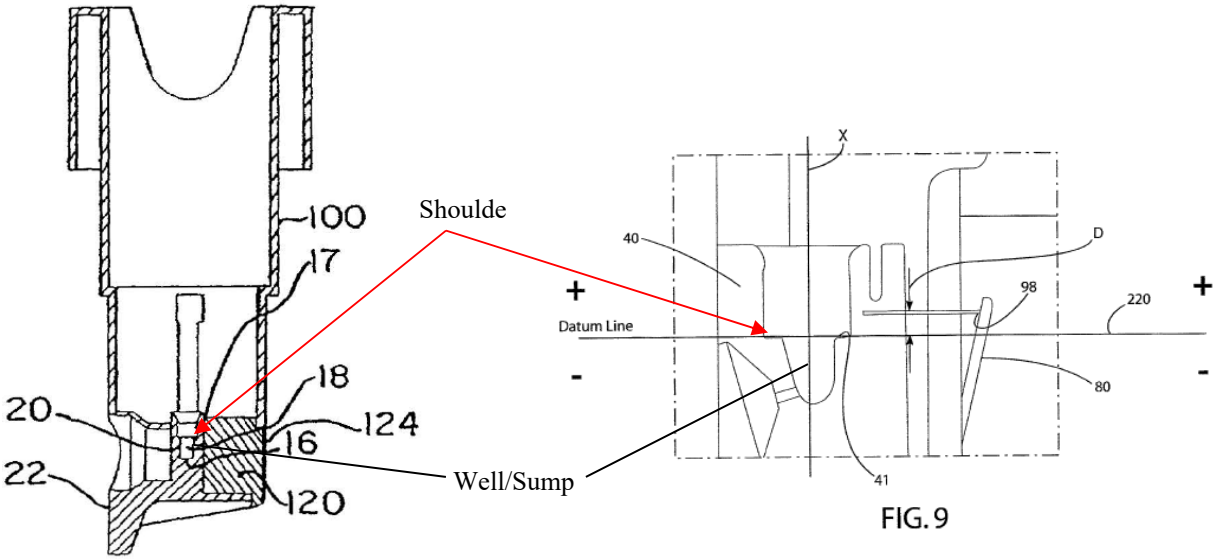
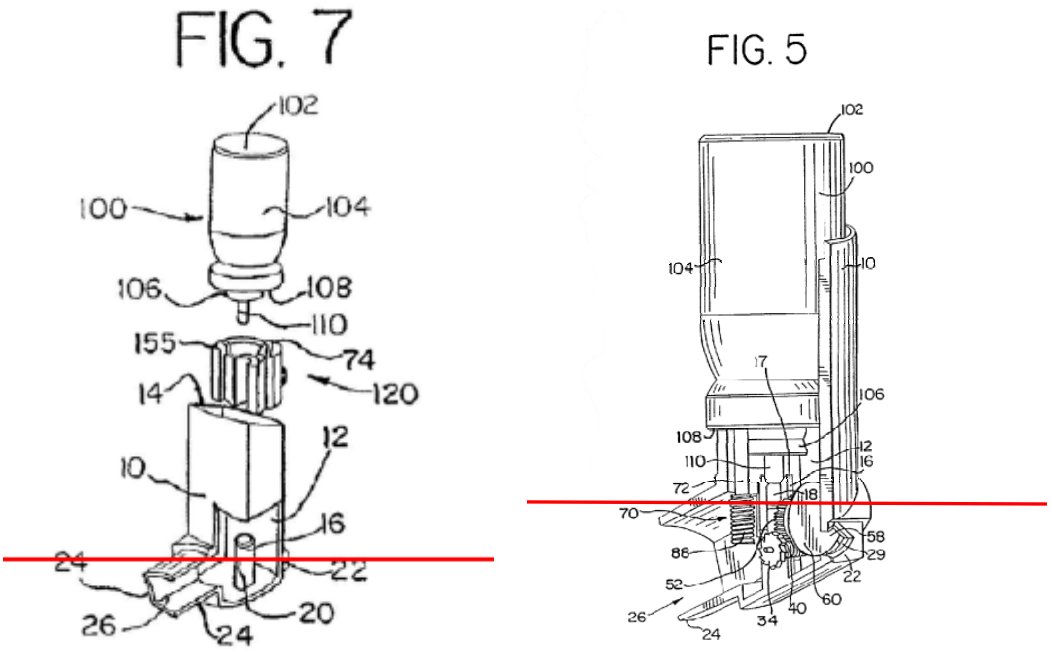


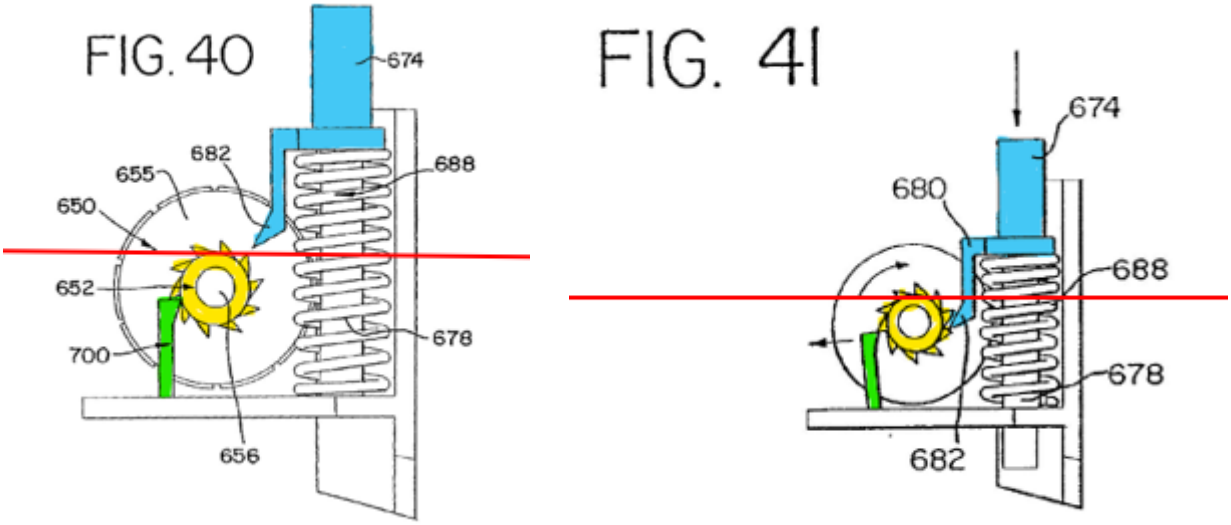
FIG. 9

84. Dr. Lewis contends that a POSA, in view of Figure 12, their own knowledge and expertise, and the information presented in the '021 Publication would be unable to extrapolate from Figure 12 to determine the location of the datum plane in other configurations. I disagree. From Figure 12, I could determine that location of the datum plane relative to the other structures of the housing—which remained consistent throughout the embodiments. This led to my extrapolation first in Figure 7, showing the datum plane in relation to the exterior of the valve stem block and the rest of the housing. Next, I considered where this datum plane would fall in Figure 5 in relation to the ratchet wheel, and extrapolated the datum plane as shown below.



85. In addition, in all embodiments, the ratchet wheel sits at the bottom of the housing surrounding the stem block. *See* '021 Publication Fig. 9, Fig. 11, Figs. 19-20, Fig. 25, Fig. 39, Fig. 48. Even if the POSA could adjust sizes, as the '021 Publication suggests, the relative positioning would reasonably remain the same. Thus, I, like any POSA, was able to also

reasonably extrapolate the datum plane line in Figures 48 (again at the top of the ratchet wheel) then to Figures 40 and 41. *See* Anderson Opening Report at ¶¶ 338 and 341.



86. As can be seen from Figures 40 and 41, as soon as the actuation pawl (blue) is depressed and brought into contact with the ratchet wheel (e.g., the first reset position) it will be just above the datum plane line. Thus, at all points after the first reset position through firing, including the canister fire configuration, the actuation pawl will be below the datum plane line. *See* '021 Publication at Figs. 40, 41; *see also id.* at [0088], [0089], [0104]; *see also supra* at ¶¶ 81-85.

87. For all these reasons, as well as the reasons set forth in my opening report, the '021 Publication anticipates claim 1 of the '156 Patent under Plaintiffs' proposed constructions.

88. Finally, Dr. Lewis opines that under Defendants' proposed constructions the '021 Publication does not disclose a "canister fire sequence," a "first reset position" or a "count configuration." I disagree for the reasons previously set forth in my opening report.

89. Dr. Lewis contends that these limitations are not satisfied because (1) my analysis of the datum plane line was flawed, (2) my analysis of Figures 40 and 41 were flawed, and (3)

the '021 Publication discloses multiple embodiments. *See* Lewis Report at ¶¶ 621-623. I disagree. As discussed in detail above, my analyses of the datum plane line and Figures 40 and 41 were the reasonable analysis that a POSA would follow. In addition, as also discussed above, the mere presence of multiple embodiments does not mean that one can never use images from one or the other where the publication, as was the case here, highlighted the similarities between the embodiments. Thus, as Dr. Lewis does not dispute my opinion on any other basis, the '021 Publication anticipates under Defendants' proposed construction as well.

2. Claims 9, 11, and 12

90. Dr. Lewis does not dispute that the '021 Publication anticipates claims 9, 11, and 12 on any basis other than his opinion that claim 1 is not anticipated. For all the reasons set forth above, claim 1 is anticipated. Therefore, if claim 1 is found to be anticipated by the '021 Publication, it is undisputed that claims 9, 11, and 12 are also anticipated under either party's proposed construction.

3. Claim 13

91. Dr. Lewis similarly does not dispute that claim 13 is anticipated, except for incorporating by reference the same opinions that he set forth with respect to claim 1. For the same reasons set forth with respect to claim 1 above, I disagree. It is therefore my opinion that claim 13 is anticipated by the '021 Publication under either party's proposed construction.

B. Claims 1, 9, and 11-13 are Anticipated by the '552 Publication

92. As an initial matter, I disagree with Dr. Lewis's characterization of my opinion as relying on "disparate descriptions and figures in the '552 Publication." Lewis Rebuttal Report at ¶ 631. To the contrary, I rely on the entirety of the '552 Publication, and the aspects of the invention described therein that are consistent throughout the various disclosed embodiments, particularly where the specification specifically states that the embodiments perform in the same

manner or differ only in a specific element. In my opinion, a POSA would recognize these similarities between embodiments and would rely on the entirety of the publication, as I have done. The mere fact that a POSA can configure the invention in a variety of shapes and sizes does not change the overarching disclosures of the publication. Moreover, while Dr. Lewis criticizes my use of the entire publication, he does not point to a particular figure that does not anticipate the claims, rather he just highlights that the publication includes multiple embodiments of the invention, as most patent publications do.

93. In addition, while Dr. Lewis states his disagreement with my interpretation of the statement "the dose counter of the present invention is based on that set out in [WO '033] except that the pawl 60 has been modified" as meaning that the only difference between the disclosures is that the pawl 60 has been modified, yet states no basis for his interpretation. *See id.* at ¶ 632. Rather he opines that a POSA would somehow infer that other changes have been made to the device, despite nothing in the publication so stating. *See id.* at ¶ 634. Dr. Lewis concludes that, despite the reference specifically stating what was changed, a POSA would presume additional changes that the '552 Publication does not articulate. A POSA would not so unreasonably speculate.

94. In addition, my reasonable interpretation is confirmed by Dr. Lewis himself. Dr. Lewis states that the '552 Publication was before the examiner during prosecution of the '156 Patent. *See* Lewis Rebuttal Report at ¶ 712. However, the reference that the Examiner considered was Bowman, the exact reference that the '552 Publication references as being the same, except for modification of the count pawl. For the '552 Publication to have been considered by the Examiner without separate analysis, it must be the same as Bowman.

1. Claim 1

95. I disagree with Dr. Lewis's opinion that the '552 Publication does not disclose firing before counting.

96. Dr. Lewis does not dispute that the specification of the '552 Publication specifically states that the dose counter of the present invention is based on that set out in [WO '033] except that the pawl 60 has been modified." Nor does he dispute that U.S. Patent No. 6,446,627 ("Bowman") is the United States patent of PCT Publication No. WO 98/28033.

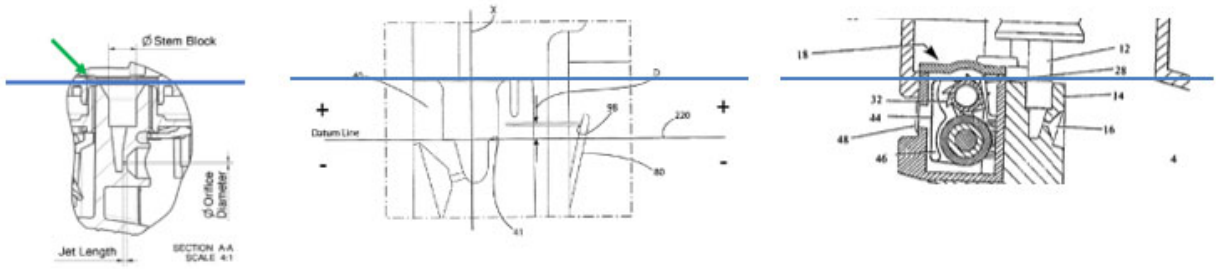
97. Dr. Lewis's argument (that Bowman and the '552 Publication do not disclose firing before counting) was already rejected, repeatedly, by the Examiner during prosecution of the claims leading to the '156 Patent. The Examiner, with whom I agree, repeatedly stated that Bowman discloses a count configuration after firing. As the Examiner explained: "The correct moment in both Bowman and the instant invention to deem counting to have occurred is when the anti-back-rotation pawl jumps over a ratchet tooth because this is when the count is locked in." October 20, 2016 Final Office Action at 3. The Examiner further cites Bowman as explaining that "the counter must only index after the metering valve has delivered its dose from the inhaler." *Id*. As stated above, it is undisputed that the dose counter in Bowman is the same as in the '552 Publication, but for modifications to count pawl 60. In addition, the '552 Publication itself confirms this stating: "The counter mechanism of the type described with reference to WO 98/28033 and in accordance with the present invention must rotate the wheel 30 of the rotary gear by exactly one tooth spacing each time the actuator is depressed. By tooth spacing is meant one tooth pitch, i.e., the radial distance between the same notational point two adjacent teeth 32 on the ratchet-toothed wheel 30. The stroke available for indexing the rotary gear is equal to the full stroke of the actuator 2. Where the metered-dose inhaler is a pressurized

inhaler, the stroke available for counting is equal to the full stroke of the medicament canister 6." '552 Publication at 10:26-11:2.

98. I disagree with Dr. Lewis's claim that the POSA "would have good reason not to interpret the '552 Publication to disclose a dose counter in which the 'canister configuration' occurs before the 'count configuration.'" Lewis Rebuttal Report at ¶ 640. First, Dr. Lewis opines that the '552 Publication teaches away from this interpretation. I disagree. As stated above, Bowman, which the '552 Publication explicitly states is the same, but for changes to the count pawl, states that firing must occur before counting. A POSA would not interpret a publication in a manner contrary to the explicit statements of the references. In addition, as discussed in detail above, Dr. Lewis has interpreted the count configuration occurring after the firing configuration to encompass split counting—that is instances where the count is committed before firing, but completed after firing. *See supra* and *infra* at ¶¶ 77, 126-127. In such an instance, there is no risk of undercounting because the count is committed before firing. *See infra* at ¶¶ 126-127. Given such a broad interpretation of counting after firing, a POSA would not understand the '552 Publication to be teaching away from a count completing after firing.

99. I disagree with Dr. Lewis's opinion that the '552 Publication does not disclose an actuator pawl below the datum plane in the canister fire configuration, when Plaintiffs' construction of datum plane is applied.

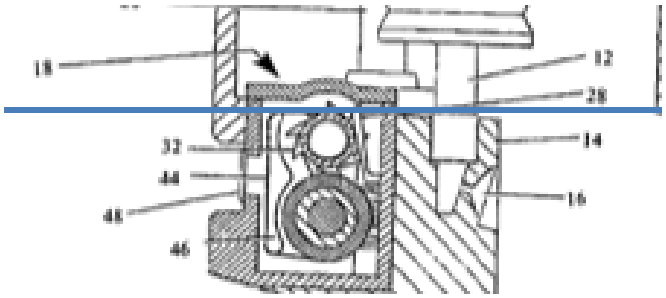
100. First, it appears that Dr. Lewis is disputing that the datum plane drawn below passes "through a shoulder of the valve stem block." *See* Lewis Rebuttal Report at ¶ 643. In my opinion, this admission confirms that Dr. Lewis drew the datum plane in the wrong place when conducting his infringement analysis, as in both instances the datum plane is drawn in the same location—the top of the valve stem block (shown in blue):



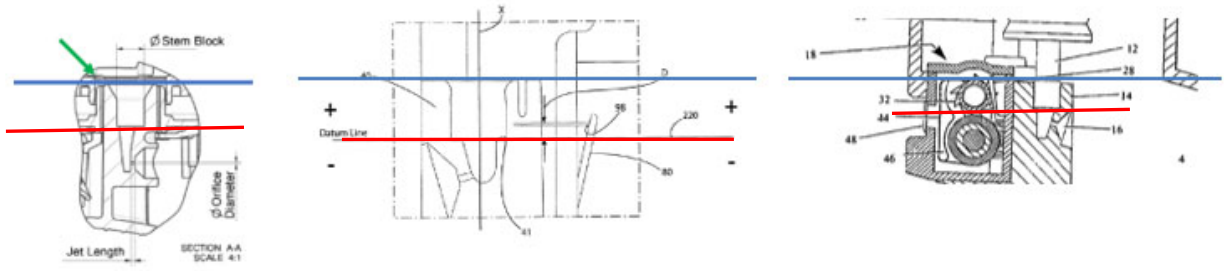
See Lewis Opening Report to Cipla at ¶ 316; Lewis Opening Report to Aurobindo at ¶ 331; '156 Patent, Figure 9; '552 Publication, Figure 2.

101. Dr. Lewis primarily disputes that the actuator pawl is below the datum plane on his incorrect assumption that a POSA would interpret the '552 Publication as changing the dose counter, and its location relative to the valve stem block, despite the '552 Publication explicitly stating that the only change was to the count pawl. As discussed above, I disagree. *See supra* at ¶ 93. A POSA would not read unstated assumptions into the disclosure based on a vague reference to studies that were not included in the reference. *Id*. Merely stating that studies were conducted does not indicate that changes were made. Indeed, because the disclosure specifically states where changes were made, a POSA would presume that, unless otherwise stated, nothing was changed between the prior art configuration (Figure 2) and the configuration in the '552 Publication.

102. Dr. Lewis next contends that the specification does not disclose Figure 2 as being in the rest or first reset position. I disagree for the reasons set forth in my opening report (e.g., the spring is not compressed, the canister valve is not compressed, the actuator pawl is at the highest point in the counter chamber). *See* Anderson Supplemental Opening Report at ¶ 53. The only direction it can move is downward. However, even though I disagree that Figure 2 could be depicting the canister fire position, even if it was, the actuator pawl is already below the datum plane line.



103. Finally, Dr. Lewis attempts to criticize my opinion for allegedly ignoring the prosecution history. I disagree. Dr. Lewis does not dispute that the Examiner compared Figure 9 of the '156 Patent to Figure 2 of Bowman (which is identical to Figure 2 of the '552 Publication). Upon comparing these figures, the Examiner agreed that the actuator pawl of Bowman was above the datum plane in the canister fire configuration. Dr. Lewis contends that this means that, contrary to what the figures plainly show, the actuator pawl is below the datum plane. He is wrong. Dr. Lewis's analysis merely confirms that his interpretation of where the datum plane can be drawn (at the top of the valve stem) must be wrong. However, if his analysis and drawing of the datum plane at the top (or head) of the valve stem block is accepted, then there is no question that the actuator pawl is below the datum plane in the fire configuration. If the datum plane is drawn correctly (shown in red) – consistent with the Examiner's analysis and Figure 9 of the '156 Patent – then, as explained in my Reports on Non-Infringement – Defendants ANDA Products do not infringe, and the '552 Publication would not anticipate. Dr. Lewis cannot have it both ways.



104. I have not opined that, under Defendants' proposed constructions, the '552 Publication anticipates claim 1 of the '156 Patent. It is, therefore, not clear what analysis Dr. Lewis is disagreeing with. However, to the extent he repeats his arguments previously set forth, I disagree for the reasons stated above.

2. Claims 9, 11, and 12

105. Dr. Lewis does not dispute that the '552 Publication anticipates claims 9, 11, and 12 on any basis other than his opinion that claim 1 is not anticipated. For all the reasons set forth above, claim 1 is anticipated. Therefore, if claim 1 is found to be anticipated by the '552 Publication, it is undisputed that claims 9, 11, and 12 are also anticipated under either party's proposed construction.

3. Claim 13

106. Dr. Lewis similarly does not dispute that claim 13 is anticipated, except for incorporating by reference the same opinions that he set forth with respect to claim 1. For the same reasons set forth with respect to claim 1 above, I disagree. It is therefore my opinion that claim 13 is anticipated by the '552 Publication under either party's proposed construction.

C. Claims 1, 9, and 11-13 Would Have Been Obvious Over the '552 Publication

107. I incorporate my analysis with respect to anticipation herein. Accordingly, my reply is limited solely to those issues unique to the obviousness inquiry.

108. I disagree that a POSA would not have been motivated to look to the '552 Publication as prior art. First, the '552 Publication is analogous art – it "relates to a metered dose inhaler" and "in particular a dose counter for a metered-dose inhaler." '552 Publication at 1:1. In addition, the '552 Publication shares a named inventor (Derek Fenlon) with the '156 Patent and both are assigned to the same company (Ivax).

1. Claim 1

109. As discussed above and in my Opening Report, the '552 Publication discloses counting before firing. *See supra* at ¶¶ 95-104. Dr. Lewis's argument about motivation and the teachings of the prior art are irrelevant because of this explicit disclosure. *See* Lewis Rebuttal Report at ¶¶ 661-662. Moreover, as discussed above, because Plaintiffs have broadly interpreted the count configuration to include counts committed to prior to firing, a POSA would not have been discouraged from pursuing a product, like the one disclosed in the '406 Publication for example, with split counting that begins prior to firing and completes after firing, and does not risk over counting. *See supra* ¶ 77.

110. I disagree that Teva's specific research and development is relevant to a non-obviousness analysis. This is truly hindsight, which I understand is impermissible. I understand that Teva was pursuing a specific, narrow goal—adjusting an existing dose counter and using existing intellectual property. *See* TEVAQVAR-00729708; TEVAQVAR-00729486-87; TEVAQVAR-0034974. A POSA more broadly developing an improved dose counter would not have faced similar design restrictions. Dr. Lewis agrees that added constraints "make the design process harder." *See* Lewis Rebuttal Report at ¶ 679. Regardless, the inventors of the '156 Patent addressed a particular dose counter (Teva's) and reached obvious solutions that were already known in the prior art. The fact that it may have taken them a significant amount of work to do so does not make their alleged invention any less obvious in view of the prior art.

111. As discussed above, Figure 2 of the '552 Publication discloses the rest or reset position. *See supra* at ¶ 102. Dr. Lewis's criticism of my reliance on Figure 2 is misplaced—a POSA would have selected Figure 2 because (1) it shows the internal structures of the device, including the valve stem block and (2) it only differs from the invention in the specifics of the count pawl design, so a POSA would understand it to disclose the same overall design as the other figures. I disagree that I "relied on Figure 2 as the basis for modification," I opined that modifying the disclosure as whole, with Figure 2 as a representative image.

112. Aside from re-stating the arguments made in connection with the anticipation argument, Dr. Lewis's primary argument is that a POSA would not have been motivated to adjust the device disclosed in the '552 Publication such that the actuator pawl is below the datum plane (when drawn pursuant to Defendants' proposed construction) in the canister fire configuration. *See* Lewis Rebuttal Report at ¶¶ 675-684.

113. Dr. Lewis attempts to support his opinion by listing a parade of horribles that may happen if the dose counting mechanism was lowered. *See* Lewis Rebuttal Report at ¶¶ 677-678. I disagree with his assessment. First, as can be seen in Figure 2, there is plenty of room within the counter chamber to lower the counter device without affecting any other aspect of the inhaler, other than corresponding lengthening of the actuator pin. *See* '552 Publication at Fig. 2. Dr. Lewis never even considers this simple adjustment. Second, the list of attributes that Dr. Lewis contends "may" be affected, are little more than the standard adjustments a POSA would expect to make when tweaking a device. As such, a POSA would expect that the minor adjustment to the location of the actuator pawl and dose counter mechanisms would result in development of a suitable device.

114. I disagree with Dr. Lewis's unsupported assessment that a POSA would not have been able to envision improving the '552 Publication. To the contrary, a POSA would have been highly motivated to improve tolerances, and thereby improve accuracy. As discussed in my opening report, lowering the placement of the actuator pawl such that the firing sequence movement is occurring near and after the firing point reduces tolerances and increases accuracy. Anderson Opening Report at ¶¶ 370-371.

115. I also disagree with Dr. Lewis's contention that the '552 Publication must list its deficiencies for a POSA to recognize them and seek to improve upon them. *See* Lewis Rebuttal Report at ¶ 681. A patent publication is not the typical place for an inventor to denigrate their own invention.

116. Finally, Dr. Lewis contends that the '552 Publication does not render "canister fire sequence," "first reset position," or "count configuration" obvious under Defendants' constructions. Lewis Rebuttal Report at ¶¶ 686-687. I disagree. As explained above, the sole difference between Figure 2 and the other embodiments was the design of the count pawl. A POSA would rely on Figure 2 to disclose positioning of the other embodiments within the housing. Because Dr. Lewis presents no new arguments, I disagree with his opinions for all the reasons set forth above.

2. Claims 9, 11, and 12

117. Dr. Lewis does not dispute that claims 9, 11, and 12 would have been obvious over the '552 Publication on any basis other than his opinion that claim 1 is not obvious. For all the reasons set forth above, claim 1 is obvious. Therefore, if claim 1 is found to be obvious over the '552 Publication, it is undisputed that claims 9, 11, and 12 are also obvious under either party's proposed construction.

3. Claim 13

118. Dr. Lewis similarly does not dispute that claim 13 would have been obvious over the '552 Publication, except for incorporating by reference the same opinions that he set forth with respect to claim 1. For the same reasons set forth with respect to claim 1 above, I disagree. It is therefore my opinion that claim 13 would have been obvious over the '021 Publication under either party's proposed construction.

D. Claims 1, 9, and 11-13 Would Have Been Obvious Over the '406 Publication

119. In my opinion, claims 1, 9, and 11-13 of the '156 Patent[1] are invalid at least because they would have been obvious under 35 U.S.C. § 103 in view of the '406 Publication.

120. As a preliminary matter, Dr. Lewis opines that a "POSA would not have reason to select the '406 Publication as the basis for designing an inhaler and/or dose counter." Lewis Rebuttal Report at ¶ 700. I disagree. First, 3M, the applicant for the '406 Publication, was a leader in design and development of inhalation devices and dose counters. As early as Spring 2008, 3M was advertising its "dose-by-dose counter," reflected in the '406 Publication. *See* Exhibit B. Although Dulera was ultimately approved after the earliest priority date of the '156 Patent, the 3M dose counter was incorporated into Dulera well before that date, indicating that POSAs would select the '406 Publication, and particularly the third embodiment for development. *See* CIPLA-BDI_0004047 and CIPLA-BDI_0004646-53.

121. Contrary to Dr. Lewis's opinions, I do not "mix and match various disclosures" from the five embodiments in the '406 Publication, nor does he identify a single such "mixing

[1] From my review of Dr. Lewis's Opening Report, I understand that Plaintiffs are no longer asserting claim 2 of the '156 Patent against Defendants. Accordingly, I reserve the right to address the validity of claim 2 later, should Plaintiffs be allowed to reassert it.

and matching" in connection with my analysis of whether the '406 Publication renders the '156 Patent obvious. *See* Lewis Rebuttal Report at ¶ 702.

1. Claim 1

122. Dr. Lewis has not disputed my opinion that Defendants' ANDA Products practice the third embodiment of the '406 Publication.

123. I have reviewed Dr. Lewis's Rebuttal Report on Invalidity regarding whether the '406 Publication renders claim 1 of the '406 Patent obvious. His opinion that it does not is premised on the alleged need for additional "data regarding the coordinates and/or dimensions of the locations of the various components that it describes." Lewis Rebuttal Report at ¶ 705. He then relies on his alleged need to "conduct[] a series of experiments on physical samples of Defendants' ANDA Products in which he measured the positions of the Defendants' actuator pawls . . . during the device's operation."[2] *Id*. at ¶ 706.

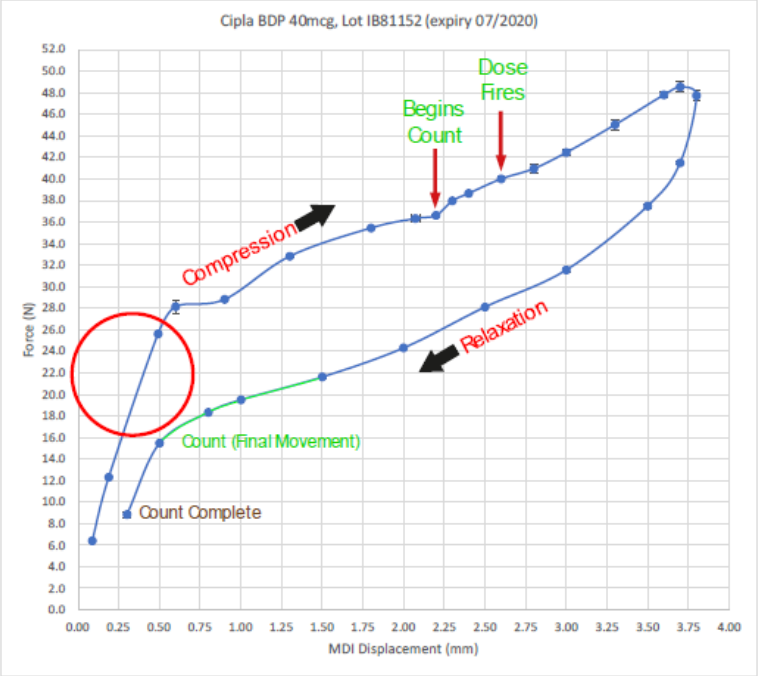
124. As, discussed above, it is undisputed that the Defendants' ANDA Products practice the third embodiment of the '406 Publication. Thus, although I disagree that Defendants' ANDA Products infringe any claim of the '156 Patent, to the extent that Dr. Lewis's opinions on infringement are correct, then his testing merely proves that, to the extent the Defendants' ANDA Products practice any limitation of claim 1 of the '156 Patent, then the '406 Publication, necessarily also discloses that limitation, at a minimum inherently.

125. Moreover, I disagree that a POSA would need additional information regarding coordinates or dimensions of various components to determine that the '406 Publication discloses each limitation of the '156 Publication. For example, the '406 Publication describes a

[2] For all the reasons set forth in my Rebuttal Report on Non-Infringement, I disagree with Dr. Lewis's characterization of the protrusion on the bottom of the indexer of Defendants' ANDA Product as an "actuator pawl."

detailed firing sequence, identical to the sequence that Defendant's ANDA Product follows. *See* Anderson Opening Report at ¶¶ 69-71, 73. To the extent Defendants' ANDA Product follows the firing sequence and reaches the configurations set forth in claim 1 of the '156 Patent, the '406 Publication discloses those same sequences and configurations.

126. Dr. Lewis opines that a POSA would have avoided developing a dose counter that satisfies the limitations of claim 1 of the '156 Patent. Dr. Lewis contends that Defendants' ANDA Product, like the '406 Publication, reaches a fire configuration ***before*** a count configuration because the count is completed on the return, ***temporally after*** firing, but ***locationally before*** the firing configuration. This can be seen in the below chart, prepared by Dr. Lewis:



See Lewis Opening Report at ¶ 122.

127. To the extent the claim is interpreted to include such configurations, a POSA would not have been discouraged from developing it. As discussed in my Opening Report, this

is exactly what the '406 Publication does and it was adopted and has been successfully used in Dulera for over a decade. In addition, this method of counting avoids the risk of undercounting, as Dr. Lewis contends that a POSA would be motivated to avoid. For example, as can be seen in the above chart, once the count begins, the device cannot fire without completing the count on its return to rest, thereby avoiding undercounting, despite the "count configuration" locationally occurring after the fire configuration. However, because the count begins, and is committed to, prior to firing, the device is more apt to overcount due to failure to compress all the way to fire, after committing to a count. This method of counting is highly accurate, as evidenced by the continued use of the '406 Publication's dose counter in Dulera, and its later inclusion in Defendants' ANDA Products.

128. I also disagree with Dr. Lewis's opinion that modifications to the '406 Publication that would result in an unsuitable device would be necessary. *See* Lewis Rebuttal Report at ¶ 707. The Defendants' ANDA Products, which Dr. Lewis contends meet every limitation of claim 1 of the '156 Patent, undisputedly practice the third embodiment of the '406 Publication, indicating that, if Dr. Lewis's infringement opinions are correct, no modification, let alone the extensive modifications Dr. Lewis opines would be necessary, were needed to practice the claims from the '406 Publication.

129. For all the reasons set forth here and in my Opening Report, it is my opinion that claim 1 of the '156 Patent is obvious over the '406 Publication.

2. <u>Claims 9 and 11-13</u>

130. Dr. Lewis does not dispute that any limitation of claims 9 and 11-12 are not disclosed by the '406 Publication other than the "dose counter as claimed in claim 1" or the "dose counter of claim 1." Thus, it is undisputed that if claim 1 of the '156 Patent is obvious over the '406 Publication, so too are claims 9 and 11-12.

131. Dr. Lewis contends that claim 13 "mirrors Defendants' proposed construction of the term 'datum plane which passes through a shoulder of a valve stem block configured to receive the medicament canister.'" Lewis Rebuttal Report at ¶ 710. Dr. Lewis also contends that, under Defendants' proposed construction, Defendants' ANDA Product infringes this claim. *See* Lewis Opening Report at ¶¶ 357-358. Although I disagree with his opinion on infringement, to the extent Dr. Lewis is correct, because the Defendants' ANDA Products practice the third embodiment of the '406 Publication, the '406 Publication also renders this claim obvious.

132. For all the reasons set forth here and in my Opening Report, it is my opinion that claims 9 and 11-13 of the '156 Patent are obvious over the '406 Publication

E. Claim 12 of the '156 Patent is Indefinite

133. I understand from counsel that a claim that is nonsensical or requires an impossibility is indefinite as a matter of law. I also understand that, in patent drafting when an element is first introduced it is introduced with an indefinite article (e.g., a or an). Subsequent references to that same element should be preceded by a definite article (e.g., the or said).

134. Dr. Lewis does not dispute that, as written, the claim language itself recites "a body" in the preamble of claim 1, referring to body of the inhaler.[3] Dr. Lewis also does not dispute that, as written, every other recitation of the "body" in claim 12 (and all claims from which it depends) use the phrase ("the body").

135. Thus, there can be no dispute that as written, claim 12 recites: "An inhaler as claimed in claim 11 in which the [body of the inhaler] includes a canister-receiving portion and a separate counter chamber, the [body of the inhaler], ratchet wheel and actuator being located

[3] Although Dr. Lewis criticizes me for not reproducing all of claim 1, nothing in claim 1 recites any other "body." Nor does any limitation of claim 1 require the ratchet wheel or the actuator to be located on a body. *See* '156 Patent at Claim 1; Lewis Rebuttal Report at fn 4.

inside the counter chamber . . . ." There is no dispute that such a reading of the claim is "nonsensical." Lewis Rebuttal Report at ¶ 723. It is also physically impossible. Thus, the claim is indefinite.

136. Dr. Lewis ignores the legal requirements of the analysis and instead rewrites the language of claim 12 to recite "a dose counter body" instead of "the body." A POSA would reject this self-serving and arbitrary rewrite of the claims.

137. **Claim Language**. First, a POSA would note that "the body" appears in multiple claims (claims 1, 2, 4, 7, 10, and 11) aside from claim 12. Not once in those claims is "the body" used to refer to anything other than the body of the inhaler. Dr. Lewis opines that because, in claim 12, the body is listed with parts of a dose counter (ratchet wheel and actuator), a POSA would necessarily understand that it is referring to a body of a dose counter. Lewis Rebuttal Report at ¶ 721. I disagree. Claim 2 refers to the actuator being disclosed relative to "the body," claim 4 refers to "the body" as including dose marker points, claim 7 recites that "the body" includes "a formation for forcing the actuator to disengage from the ratchet wheel," and claim 10 claims a dose counter in which the count pawl (which claim 1 indicates is part of the dose counter) is "substantially fixedly mounted on the body." Thus, a POSA reading the claims, would not find it clear whether "the body" (e.g., the body of the inhaler) is also part of the dose counter.

138. Dr. Lewis opines that "Mr. Anderson's analysis is contrary to the approach that the POSA would have taken in understanding the claim language. Mr. Anderson appears to assume that the phrase 'the body' to have the same meaning each time that it was used, and then based on that assumption, asserts that Asserted Claim 12 is structurally impossible. [ ] By contrast, the POSA would have understood common terms, such as 'body,' could have different

meanings based on the contexts in which they were used, and based on those contexts, would select the appropriate ones. Following those principles, the POSA would understand that the second usage of the term 'the body' must refer to the dose counter 'body,' in part because the contrary conclusion would yield a nonsensical result." Lewis Rebuttal Report at ¶ 723.

139. I understand that Dr. Lewis's opinion is not based on the law, particularly the law surrounding antecedent basis. In my opinion, a POSA would not eschew the legal principles surrounding claim interpretation in favor of principles applied in interpreting scientific or technical papers or presentations. *See* Lewis Rebuttal Report at ¶ 724.

140. **Specification.** I disagree with Dr. Lewis's attempt to disregard the fact that the specification uses "body" over 70 times to describe a variety of things that may have bodies. *See* Anderson Opening Report at ¶ 412. Given the lack of context provided by the claims (discussed above) and the specification, a POSA would not arbitrarily pick a meaning for "body" from one of the many uses in the specification.

141. **Prosecution History.** Dr. Lewis attempts to rely on the prosecution history to support his opinion. However, he fails to identify a single instance that the Prosecution History informs a POSA what is mean by the second "body" in claim 12.

142. For all the reasons set forth here and in my Opening Report, it is my opinion that claim 12 of the '156 Patent is indefinite.

XV. INVALIDITY OF THE '808 PATENT

A. Anticipation of the '808 Patent

1. Anticipation of the '808 Patent by the '552 or '950 Publications

a. Claim 1

143. Dr. Lewis incorrectly asserts that that my analysis of anticipation of claim 1 by the '552 Publication relies on multiple references, *i.e.*, both the '552 Publication and the '950

Publication. *See* Lewis Rebuttal Report at ¶ 735. He is incorrect. Counsel has explained to me that in an anticipation rejection, multiple references may be used to show an inherent characteristic of a teaching of the primary reference. The '552 Publication makes clear that the interaction of the split hub and nubs with the stock bobbin of Figure 6 is to cause the counter tape to be held taut: "Fig. 6 shows an exploded view of the dose counter 18 showing in addition to the previously described components, the stock bobbin 68 which is held taut by the action of the split hub 70. The split hub 70 avoids the need for a clutch spring as set out in WO 98/28033." (Page 9, lines 9-12); "The counter tape 44 is held taut by the action of the split hub 70 on which is mounted the stock bobbin 68." (Page 10, lines 6-8). Figure 6, reproduced below, discloses the nubs on the split hub 70.

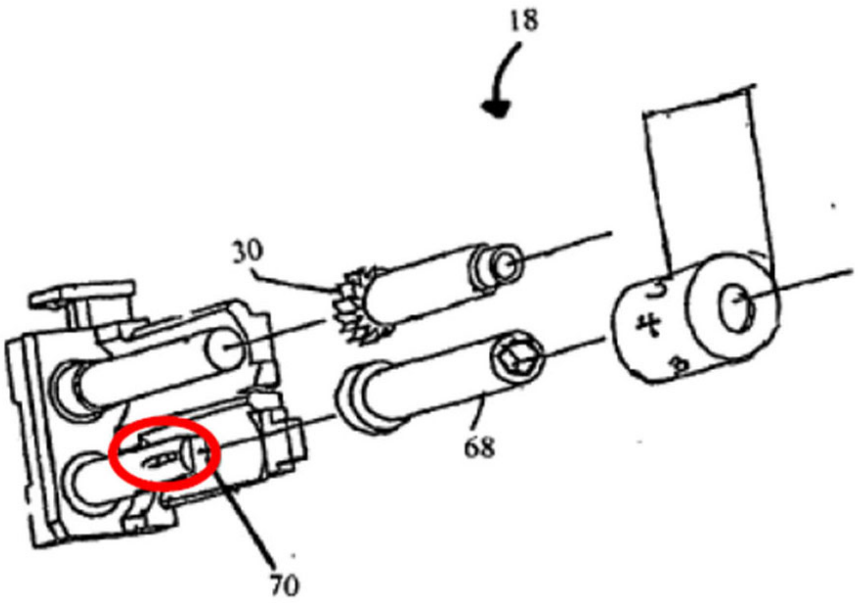


Fig. 6

144. As I previously explained at paragraph 430 of my opening report, one of skill in the art would readily recognize that the arrangement of protrusions on a split hub inserted into the inner channel of bobbin 68 would result in the protrusions contacting the interior surface of

the stock bobbin 68 that would modulate motion of the tape. As I explained at paragraph 430 of my report, the '950 Publication confirms this understanding of the interaction between the split hub and the inner channel of the bobbin 68. This demonstrates that this characteristic disclosed in the '552 Publication is an inherent characteristic.

145. Dr. Lewis also incorrectly asserts that in my analysis of the '552 Publication I mixed and matched embodiments. Lewis Rebuttal Report at ¶ 735. This is simply incorrect and Dr. Lewis does not identify a single instance of such "mixing and matching" in connection with my analysis of whether the '552 Publications anticipates the '808 Patent. He refers to section VI.B.1.a.1, and paragraph 657 in particular, to support this assert for my analysis of the '552 Publication. I have reviewed these passages and disagree with his assertion that there is a mixing and matching of different embodiments.

146. In his analysis of anticipation by either the '552 or the '950 Publication, Dr. Lewis is inconsistent in has analysis compared to his infringement report. For example, it is inconsistent for Dr. Lewis to assert in his validity report that the interaction between the nubs on the split forks and the inner surface of the bobbin does not result in incremental movement when he argues (albeit, incorrectly) that the same interaction between the leaf spring and the smooth surface of the units teeth ring in his infringement report results in incremental movement. Given the lack of wavelike forms on the smooth surface of the units teeth ring, it is clear that, especially under Dr. Lewis's interpretation, the nubs would similarly restrain movement to incremental movement.

147. Dr. Lewis is inconsistent in how he interprets the regulator and incremental movement limitations in his Opening Report on infringement, his Rebuttal Report on invalidity and his explanation of the prosecution history of the '808 Patent. His understanding of

incremental movement in the infringement report differs from that in his invalidity report. In his infringement report, Dr. Lewis asserts that the leaf spring is the claimed regulator and "could comprise 'a wavelike engagement surface with concavities which engage against control elements in the form of protrusion on resilient fork of a split pin.'" Lewis Opening Report at ¶¶ 420-421. However, Dr. Lewis also asserts that "to the extent that the '808 Patent describes the regulator as having a wavelike engagement surface, that was not an essential aspect of the invention." *Id*. at ¶ 420.

148. Defendants' leaf spring is in compression against a smooth surface of the units teeth ring. That surface does not vary over its 360 degree circumference, much less have a wavelike engagement surface. Similarly, the nubs on the split hub disclosed in the '950 and '552 Publications are in compression against a smooth surface of the inner diameter of the bobbin. That surface does not change over its 360 degree circumference. To the extent Lewis asserts that the leaf spring corresponds to the regulator of claim 1 and claim 1 is infringed, the split hubs with nubs of the '950 and '552 Publications similarly anticipate the regulator of claim 1.

149. Dr. Lewis is also inconsistent in his interpretation of incremental movement. In his Opening Report he essentially asserts that the leaf spring modulates the dose counter to incremental movement because it applies a force against the units teeth ring that varies during actuation. He even notes that with the medicament canister removed the dose counter components continue to provide a resistive force against the downward motion of the medicament canister. *See* Lewis Opening Report at fn 7, page 180. The interaction between the split hub with nubs and the stock bobbin of the '552 and '950 Publications with the medicament canister similarly would continue to provide a resistive force against the downward motion of the medicament canister. To the extent Dr. Lewis asserts that the leaf spring's resistive force results

in incremental movement, and claim 1 is infringed, the resistive force provided by the split hubs with nubs in the stock bobbin disclosed in the '950 and '552 Publications anticipate the regulator with incremental movement of claim 1.

150. Dr. Lewis's reliance on the Patent Trial and Appeal Board ("PTAB") decision in the appeal of a rejection of the '808 Patent based on the '950 Publication further demonstrates the inconsistency in how he is interpreting incremental movement. Lewis Rebuttal Report at ¶¶ 744-745. The PTAB overturned a rejection of the claims based on the '950 Publication failing to disclose a regulator capable of regulating motion in the manner recited by claim 1. In its decision, the PTAB referred to the hexagonal structure of the bobbin and stated that "even if the evidence adequately supported that O'Leary nubs 146 interact with the hexagonal structure or some other corresponding structure of bobbin 132, it is not clear that the interaction would, as the Examiner concedes, necessarily result in incremental movement." '808 Patent Prosecution History, Sept. 20, 2019 PTAB Decision at 5. The PTAB decision quoted by Dr. Lewis makes clear that some structure is needed to provide the incremental movement. However, Dr. Lewis's Opening Report essentially asserts that no such structure is needed in the dose counter to show infringement while arguing in his Rebuttal Report that there is no anticipation or obviousness because such structure is missing in Figures 6 and 15 of the '552 and '950 Publications, respectively. Dr. Lewis appears to be arguing that the interaction between the leaf spring and the smooth surface of the units teeth ring provides that structure and results in incremental movement. Because the interaction between the leaf spring and the smooth surface of the units teeth ring is essentially the same as that of the interaction of the nubs on the split fork 70 and the stock bobbin 68, based on Lewis's arguments the '552 and '950 Publications disclose the regulator modulating incremental movement as required by claim 1.

151. The Lewis Rebuttal Report also is inconsistent in its description of the difference between the action of the leaf spring on the surface of units teeth ring and the interaction of the split fork with the nubs. At paragraph 756, Dr. Lewis explains that "continuous or frictional resistance like that provided by the tape stock bobbin/split hub combination disclosed in the '552 Publication and/or radial axis nubs disclosed in the '950 Publication does not necessarily modulate the counter display to incremental movements." Initially I note that both the '552 and '950 Publications disclose the same configuration: a combination of tape stock bobbin mounted on a split hub with radial axis nubs. I have reproduced Figure 6 of the '552 Publication and Figure 15 of the '950 Publication below.

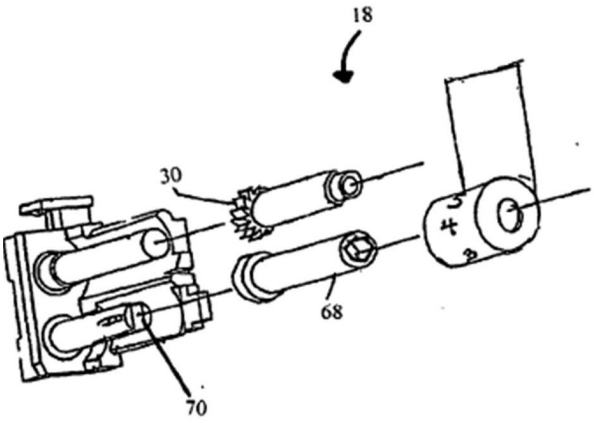


Fig. 6

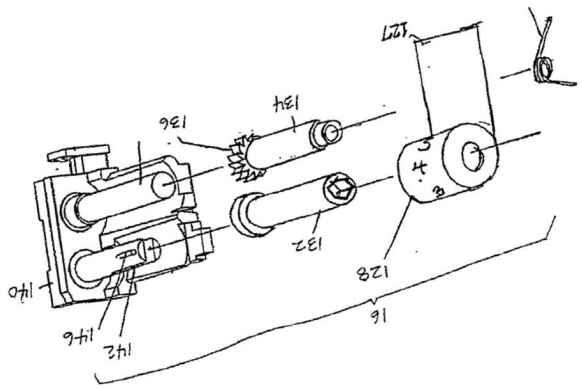


Fig. 15

152. Both figures show the combination of a tape stock bobbin/split hub with radial axis nubs. The only differences between the two figures is the inclusion of a spring in Figure 15. Dr. Lewis attempts to differentiate these figures from the '808 Patent based on the alleged lack of wave-like structures. However, as Dr. Lewis has already admitted, "to the extent that the '808 Patent describes the regulator as having a wavelike engagement surface, that was not an essential aspect of the invention," and has asserted that products (like Defendants' ANDA products) infringe even in the absence of such structures, it is clear that they do not perform the necessary

regulation, but rather that the nubs present in both the prior art and the '808 Patent perform that function. Lewis cannot opine that wavelike structures are responsible for incremental movement to avoid invalidity, and simultaneously claim that they are "not an essential aspect of the invention" for infringement.

153. Dr. Lewis's reliance on the appeal decision of the '808 Patent in his Rebuttal Report conveniently ignores numerous statements in the appeal to the PTAB that contradict his Opening Report. *See* Lewis Rebuttal Report at ¶744. For example, the PTAB Appeal Brief characterizes the claimed regulator as "regulating the counter display with incremental movements, instead of a constant application of force … regulating the motion of the counter display with incremental movements achieves at least two objectives: it prevents undesirable movement of the counter display if the inhaler is dropped, and avoids the use of high friction against the counter display." '808 Patent Prosecution History, May 21, 2018 Appeal Brief at 3. Dr. Lewis is inconsistent when arguing that, for infringement, the leaf spring applies a wavelike motion in his Opening Report when it actually applies continuous/constant high friction against the units teeth ring while, in his invalidity report, he cites the Appeal Decision to differentiate the claims from O'Leary, which similarly applied friction against the shaft that the counter display tape was wrapped upon.

154. Dr. Lewis is inconsistent between his validity report and his Opening Report and is also inconsistent with the Applicants' PTAB Appeal Brief as to the structure of the claimed regulator. Applicants' PTAB Appeal Brief during prosecution of the '808 Patent argued that the nubs, which the Examiner equated to the regulator, "provide added friction as they are urged against the bobbin. There are no teachings in O'Leary that suggest the nubs are supposed to function as 'connecting parts' or to complement another feature, as stated by the Examiner."

'808 Patent Prosecution History, May 21, 2018 Appeal Brief at 6. Dr. Lewis ignores this in his invalidity report when he argues that the leaf spring can function as the regulator. The leaf spring does not function as a "connecting part" or "complement some other feature." The leaf spring is in compression and slides across the smooth, lower surface of the units teeth ring, in the same manner as the nubs are in compression and slide against the smooth surface of the bobbin. He also ignores these similarities in his infringement report in asserting that the leaf spring is the regulator and provides incremental movement. *See* Lewis Rebuttal Report at ¶ 412.

155. Dr. Lewis also is inconsistent in asserting that the '552 and '950 Publications do not "otherwise disclose or suggest anything that regulates the motion of the counter display to incremental movement." Lewis Rebuttal Report at ¶ 748. The '552 Publication discloses a driver28 that advances the wheel 30 with ratchet teeth 32 in an incremental movement, a pawl 60 prevents reverse rotation, and nubs on the split hub that keep the display tape taut. Contrary to Dr. Lewis, the combination of the driver 28, ratchet teeth 32 on wheel 30, and split hub with nubs against the inside of the bobbin results in regulating the motion of the counter display to incremental movements.

156. Dr. Lewis cannot now argue that the incremental movement must be caused at the first station of the counter display. Dr. Lewis stated in his Opening Report, there is no requirement that the regulator "directly acts upon" the counter display. *See* Lewis Opening Report at ¶¶ 415-416. He then opined that the regulator acts directly on the counter display only in certain embodiments of the invention, which implies that other embodiments do not require the regulator to act directly upon the counter display. *Id.* at ¶ 417.

157. Dr. Lewis also ignores the Patentee's description of the force applied by the radial nubs engaging the smooth inner shaft of the bobbin demonstrating how similar it is to the alleged

regulator's engagement with the smooth lower surface of the units teeth ring in Defendants' ANDA Products. In its Appeal Brief the Patentee argued that "a skilled artisan may interpret O'Leary as describing a device wherein the radial nubs engage a smooth inner shaft of the bobbin to provide continuous resistance force as the bobbin rotates, in order to prevent free spooling of the bobbin." '808 Patent Prosecution History, May 21, 2018 Appeal Brief at 7. "The type of 'resilient resistance' described by O'Leary is commonly applied in numerous contexts, for example, common brake pads on a bicycle wheel provide resilient resistance against a smooth wheel rim, thereby slowing the rotation of the wheel." *Id.* "*In fact, the claimed invention solves a problem presented by the arrangement taught by O'Leary, in which the protruding nubs provide constant friction against the bobbin.*" *Id.* (emphasis in original). Like the protruding nubs and the bobbin, the leaf spring provides a constant friction against the smooth surface of the units teeth ring. Thus, to the extent Dr. Lewis opines that the leaf spring is encompassed by the regulator limitation of claim 1, then both the '552 Publication and the '950 Publication similarly disclose regulators encompassed by claim 1.

158. Dr. Lewis is inconsistent in arguing that complementary features are absent in the '552 and '950 Publications to provide incremental movement. *See* Lewis Rebuttal Report at ¶ 747. The PTAB decision states that even if the hexagonal head, which is a complementary feature to the nubs, extended all the way along the length, the Board was unsure if that arrangement would provide incremental movement. '808 Prosecution History, September 20, 2019 PTAB Decision at 5. In his Opening Report at paragraph 412, Lewis states that the canister presses down on the indexer and engages the units teeth ring, causing it to rotate. The units teeth ring then causes the units display ring and tens cone to rotate. Lewis Opening Report at ¶ 412. But if these are amongst the complementary features that provide incremental movement for

infringement, they are no different from the driver, pawl, and ratchet teeth of the '552 and '950 Publications in combination with the split hub and axial nubs in compression against the inner surface of the bobbin shaft. Dr. Lewis is inconsistent in how he treats the arrangement of these components for purposes of infringement and validity.

159. Dr. Lewis states that the split hub maintains tension generally, not incrementally. *See* Lewis Rebuttal Report at ¶ 749. Lewis also states that nothing in the '552 or '950 Publications suggests that the dose counter moves incrementally, much less that the split hub in this body has any effect in achieving that outcome. This is incorrect. The figures of the '552 and '950 Publications clearly show that the nubs on the split hub are resisting incremental movement. The driver 28 and pawl 60 interact with the wheel 30 and ratchet teeth 32 to provide incremental movement of the tape, which the nubs/split hubs resist. In this manner, the combination of these components provides the incremental movement required by claim 1. Claim 1 does not require any more structure than that. As I explained above, Dr. Lewis's Opening Report makes clear that the regulation of incremental movement is not required to be only at the counter display.

160. Dr. Lewis also asserts that the '808 Patent discloses multiple embodiments of the regulator. Lewis Rebuttal Report at ¶¶ 750-752. However, his citations to the '808 Patent do not disclose any embodiments other than a regulator in the form of a shaft having "a wavelike engagement surface with concavities which engage against the control elements in the form of protrusions in the resilient forks of a split pin." Dr. Lewis points to no other embodiments of the regulator other than the wavelike engagement surface with concavities. In so doing, Dr. Lewis is inconsistent in his Opening Report where he asserts infringement when no such structure is present in the Defendants' ANDA Products and in his Rebuttal Report where he asserts that such

structure is missing from the '552 and '950 Publications but is needed for anticipation and obviousness.

161. Thus, for at least the reasons set forth above, and in my Opening Report, claim 1 of the '808 Patent is anticipated by the '552 Publication and the '950 Publication.

B. Obviousness of the '808 Patent

1. Obviousness of the '808 Patent by either of the '552 and '950 Publications and the POSA's Knowledge

a. Claim 1

162. As a preliminary matter, Dr. Lewis opines that a "POSA would not have had a reason to select the '552 Publication as the basis for designing an inhaler and/or dose counter." *See* Lewis Rebuttal Report at ¶ 781. Dr. Lewis makes a similar statement for the '950 Publication. *See* Lewis Rebuttal Report at ¶ 802. This is the wrong analysis. A POSA is deemed to have knowledge of the prior art, including the '552 Publication and the '950 Publication, and Dr. Lewis does not contest that the '552 Publication and the '950 Publication are both analogous art.

163. Dr. Lewis also opines that a POSA would not have had a reason to modify the '552 Publication with a reasonable expectation of success. *See* Lewis Rebuttal Report at ¶ 782. Dr. Lewis makes a similar statement for the '950 Publication. *See* Lewis Rebuttal Report at ¶ 803. I disagree. The only difference between the dose counter of the '552 and '950 Publications and that disclosed in the '808 Patent appears to be the wavelike concavities on the inner surface of the bobbin. This is a very minor modification to the bobbin that would have been quite simple for the POSA. All that is required is a slight modification to the mold used to make the bobbin.

164. Dr. Lewis asserts that neither the '552 Publication nor the '950 Publication in combination with the POSA's knowledge would render the asserted claims obvious. I incorporate here my discussion above as to why the disclosures of both the '552 Publication and the '950 Publication render claim 1 anticipated. For the same reasons, they render claim 1 obvious.

165. For all the reasons set forth here and in my Opening Report, it is my opinion that claim 1 of the '808 Patent would have been obvious over the '552 or '950 Publications in combination with the POSA's knowledge.

b. Claims 27 and 28

166. I disagree with Dr. Lewis's opinion that neither the '552 Publication and/or the POSA's knowledge or the '950 Publication and/or the POSA's knowledge would not render obvious the resistance force values of claims 27 and 28 for all the reasons set forth in my Opening Report.

2. Obviousness of the Asserted Claims of the '808 Patent Over the '406 Publication

167. As explained in my Opening Report, the '406 Publication in view of the knowledge of a POSA renders obvious the asserted claims of the '808 Patent.

168. As a preliminary matter, Dr. Lewis opines that a "POSA would not have had a reason to select the '406 Publication as the basis for designing an inhaler and/or dose counter." *See* Lewis Rebuttal Report at ¶ 823. This is the wrong analysis. A POSA is deemed to have knowledge of the prior art, including the '406 Publication, and Dr. Lewis does not contest that the '406 Publication is analogous art. Second, 3M, the applicant for the '406 Publication, was a leader in design and development of inhalation devices and dose counters. As early as Spring 2008, 3M was advertising its "dose-by-dose counter," reflected in the '406 Publication. *See*

Exhibit B. Although Dulera was ultimately approved after the earliest priority date of the '808 Patent, the 3M dose counter was incorporated into Dulera well before that date, indicating that POSAs would select the '406 Publication, and particularly the third embodiment for development. *See* CIPLA-BDI_0004047 and CIPLA-BDI_0004646-53. Notably, Dr. Lewis also has not disputed my opinion that Defendants' ANDA Products practice the third embodiment of the '406 Publication.

169. Dr. Lewis asserts that I mix and match various disclosures from the five embodiments of dose counters of the '406 Publication. Contrary to Dr. Lewis's opinions, I do not "mix and match various disclosures" from the five embodiments in the '406 Publication, nor does he identify a single such "mixing and matching" in connection with my analysis of whether the '406 Publication renders the asserted claims of the '808 Patent obvious. *See* Lewis Rebuttal Report at ¶ 824-825.

1. Claim 1

170. In addressing Claim 1, Dr. Lewis points only to the limitation that recites "wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movement." *See* Lewis Rebuttal Report at ¶¶ 826-828.

171. As discussed above, it is undisputed that the Defendants' ANDA Products practice the third embodiment of the '406 Publication. Thus, although I disagree that Defendants' ANDA Products infringe any claim of the '808 Patent, to the extent that Dr. Lewis's opinions on infringement are correct, then his opinions on infringement merely prove that, to the extent the Defendants' ANDA Products practice any limitation of claim 1 of the '808 Patent, then the '406 Publication, necessarily also discloses that limitation, at a minimum inherently. As discussed above, Dr. Lewis attempts to avoid this problem by asserting different requirements

for infringement and invalidity. I understand that it is improper to treat a patent different for analyzing infringement and invalidity.

172. I disagree with Dr. Lewis's opinion at paragraph 828 that the POSA would not have understood the disclosure of the '406 Publication to disclose and/or render obvious this regulator limitation. Dr. Lewis first implies that, based on the '406 Publication as providing only two-dimensional disclosures, a POSA would not understand the disclosure of the '406 Publication. I disagree that two-dimensional disclosures are difficult for the POSA to understand and question why he would raise this objection to the '406 Publication when the '808 Patent provides only two-dimensional disclosures. Dr. Lewis then argues that the '406 Publication is lacking because it fails to disclose the purpose of the leaf spring or that the leaf spring prevents the dose counter from counting if the inhaler device is dropped on a hard surface. The POSA does not need the '406 Publication to disclose the purpose of the leaf spring because the purpose would be readily apparent to the POSA from the disclosure of the '406 Publication. Moreover, if Dr. Lewis's infringement analysis is correct, then the leaf spring when used as disclosed in the '406 Publication, inherently performs the role of a "regulator."

173. In his rebuttal report Dr. Lewis asserts that the '406 Publication does not provide the POSA with a reason to develop an inhaler and dose counter that satisfies the limitations of the '808 Patent with a reasonable expectation of success. *See* Lewis Rebuttal Report at ¶ 828. However, because Defendants' ANDA Products use the dose counter of the third embodiment of the '406 Publication, indicating that, if Dr. Lewis's infringement opinions are correct, no modification, let alone the extensive modifications Dr. Lewis opines would be necessary, were needed to practice the claims from the '406 Publication.

174. For all the reasons set forth here and in my Opening Report, it is my opinion that claim 1 of the '808 Patent is obvious over the '406 Publication.

2. Claims 27 and 28

175. I disagree with Dr. Lewis's opinion that the '406 Publication and/or the POSA's knowledge would not render obvious the resistance force values of claims 27 and 28 for all the reasons set forth in my Opening Report.

C. Invalidity of the Asserted Claims of the '808 Patent based on Lack of Written Description and Lack of Enablement

176. I disagree with Dr. Lewis's explanation as to how the disclosure of the '808 Patent provides adequate written description and enablement for a dose counter with multiple displays or a multi-part counter display. To argue adequate written description and enablement for a dose counter with two displays, Dr. Lewis relies on the Abstract of the '808 Patent and passages at column 2, lines 44-53 and column 8, lines 31-50. *See* Lewis Rebuttal Report at ¶¶ 838-840. I have reviewed these passages and nothing in them provides adequate written description and enablement for a dose counter that, for example, has "multiple counter displays" as Lewis alleges in his report. *See* Lewis Rebuttal Report at ¶¶ 838, 839. These passages are too general to provide any meaningful support.

177. Dr. Lewis appears to disagree with me that the '808 Patent discloses a dose counter with only a single tape display, not multiple displays or multiple tape displays that can move independently. *See* Lewis Rebuttal Report at ¶ 841. However, he fails to point to any passage or figure that shows any display other than a single tape that passes between two bobbins. He certainly does not point to any disclosure of multiple displays or multiple displays that move independently.

178. For all the reasons set forth here and in my Opening Report, it is my opinion that claim 1, under Plaintiffs' proposed construction of "counter display arranged to indicate dosage information," is not enabled and lacks written description support.

XVI. REVISION OR SUPPLEMENTATION

179. I reserve the right to modify and supplement this report based on information that may subsequently become available in this matter, and to respond to issues yet to be raised in the litigation. I reserve the right to change or formulate new opinions if there is a material change in the law concerning patent infringement between now and trial.

XVII. DEMONSTRATIVE EXHIBITS

180. If called to testify at trial I may prepare demonstrative exhibits, such as charts and graphs, to further explain my opinions.

Dated July 12, 2022

EXHIBIT A

EXHIBIT A

MATERIALS CONSIDERED IN REPLY REPORT OF GREGOR ANDERSON ON INVALIDITY

Description	Bates No.
Anderson Opening Report dated April 29, 2022 and the materials cited therein, including Materials Listed in Exhibit B	
Supplemental Anderson Opening Report dated May 24, 2022 and the materials cited therein, including Materials Listed in Exhibit B	
Anderson Rebuttal Report dated June 14, 2022 on behalf of Cipla and the materials cited therein, including Materials Listed in Exhibit A	
Anderson Rebuttal Report on Secondary Considerations dated June 14, 2022 and the materials cited therein, including Materials Listed in Exhibit A	
Opening Expert Reports of Dr. David Lewis dated April 29, 2022 to Cipla and Aurobindo and the materials cited therein	
Opening Expert Reports of Dr. Reynold Panettieri dated April 29, 2022 to Cipla and Aurobindo and the materials cited therein	
Rebuttal Report of Dr. David Lewis dated June 14, 2022 to Cipla and Aurobindo and the materials cited therein	
[redacted]	
3M Letter to FDA	CIPLA-BDI_0004047
CIPLA PDR	CIPLA-BDI_0004411-4705
3M Drug Delivery Systems, 10 Ways to Protect your pMDI Product	
Report No. 06-RD-31, Ivax Pharmaceuticals Ireland, Qvar Counter Patient Information Sticker Proposal December 16, 2006, Walsh Deposition Exhibit 10	TEVAQVAR-00729706-713
Teva Albuterol MDI 200 Mechanical Dose Counter Indicator Feasibility Study, Walsh Deposition Exhibit 11	TEVAQVAR-00729485-495
Albuterol HFA MDI , History of Product Development, Walsh Deposition Exhibit 12	TEVAQVAR-0034974-75
’808 Patent Prosecution History	
’156 Patent Prosecution History	

EXHIBIT B

3M Drug Delivery Systems
INHALATION SYSTEMS & COMPONENTS

10 Ways to Protect Your pMDI Product

White Paper / Spring 2008

Methods that help reduce risk and drive preference in a competitive market.

ENABLING YOUR SUCCESS.

3M

Introduction

With the increasing cost of drug development, advancing regulatory guidelines to protect public health and the threat of generic substitution as patents protecting molecules and delivery systems expire, pharmaceutical companies are under increasing pressure to protect and maximize revenue from existing product portfolios. In such a closely competitive environment, the integration of sound drug delivery management practices is critical to the ongoing success of a molecule.

Three key areas must be addressed:

- *Reducing the risk of product failure during development*
- *Driving preference in patients and prescribers*
- *Protecting the molecule from substitution by competitor or generic alternatives*

By following the ten best practices in this paper, you can help reduce risk, drive preference, and protect your molecule from substitution, thereby maximizing your product's chances for long-term commercial success.

10 Best Practices Table of Contents

SECTION 1

Enable dose tracking for patients

Running out of medication is a major concern for patients. Inclusion of a dose counter in pMDIs addresses that concern and helps drive preference.

Pressurized metered-dose inhalers (pMDIs) have been around for more than fifty years and are generally regarded as the preferred method of drug delivery to the lungs for the treatment of conditions such as asthma, emphysema and chronic bronchitis. Advantages of this delivery method include reliability, accurate dosing, convenience and low cost. However, it is difficult for patients to keep track of the number of doses remaining in their inhaler, and patients have often resorted to primitive methods such as immersing the aerosol canister in water or keeping a written record to help them determine when to replace their inhalers. A survey conducted in the U.S. in 2003[1] found that only 36% of 342 adult asthmatics reported having been told to keep track of their pMDI doses. Additionally, 25% had found their inhaler to be completely empty when they needed it resulting in 8% needing emergency services.

Given this clear patient need for dose tracking mechanisms, the FDA published guidance in 2003 expecting new pMDI products to include an accurate means of informing patients as to the remaining number of doses left in their device. This mechanism must be an integral part of the inhaler (not an add-on) and be designed to count downwards to zero, enabling patients to know when the inhaler is reaching the end of its life. Other key criteria in the guidance can be seen in Figure 1-1.

The FDA guidance has generated a great deal of interest around dose-counting mechanisms and, while these features are neither compulsory for other regulatory bodies nor a requirement for existing products, many pharmaceutical companies are considering including a counting mechanism across their product range to help them differentiate their products from other inhalers. Additionally, by utilizing the same methods of operation, display options (individual dose by dose tracking or dose indication) and product design across a product range, a consistent “family feel” can be achieved, further differentiating products in the market.

The 3M™ Integrated Dose by Dose Counter has been designed to meet the requirements of regulators, pharmaceutical companies and patients alike. It incorporates a number of significant features including an ergonomic and robust design that has been integrated into the actuator to maintain a familiar inhaler look and feel for patients, as well as ensure compatibility with existing manufacturing lines. It utilizes a split-count design principle to match dose counter actuation as closely as possible to valve travel for solid accuracy while the individual dose-by-dose count and clear display addresses the patient’s need to know when their inhaler is low. This gives patients the information they need to obtain a refill in a proactive manner, delivering clear benefits not only in peace of mind but also in condition management by allowing patients and care givers, including parents, to monitor use. This additional monitoring benefit was highlighted as a positive element during research in which the 3M Integrated Dose by Dose Counter was tested by key patient groups, including children and the elderly, to ensure the dose counter design not only met patient expectations but would enhance their experience of using a pMDI and increase their confidence in managing their disease.

Figure 1-1 Key Criteria for Dose Counter Design

Figure 1-1

[1] N. Sander, S Fusco-Walker, J. McElvain and B. Chipps (2006). Dose-counting and the use of pressurized metered-dose inhalers: running on empty. Annals of Allergy, Asthma and Immunology, 97, 1, pp34-38

FDA GUIDANCE	TECHNICAL REQUIREMENT	3M DOSE COUNTER
"a clear indication of when an MDI is approaching the end of its recommended number of actuations"	Individual dose by dose counter or dose indicator	Individual dose by dose counter
"integral part of the MDI canister and/or actuator, and not simply an add-on that can be removed and used multiple times"	Integral to the canister or actuator	Integral to the actuator
"Dose counters should be engineered to reliably track actuations"	Specifically, must avoid undercounting	Displacement driven split-count principle drives accuracy
"in-use studies…should address issues related to ergonomics, ruggedness, and accuracy"	Demonstrated ruggedness, accuracy and ergonomics in clinical use	Designed to be robust in the hands of patients as well as during shipping and transportation
"A lock-out mechanism to prevent doses beyond the labeled number of actuations would be an optional feature of dose counters"	Prevents patient using inhaler past zero. Not recommended for bronchodilator rescue medications	Does not include this optional feature

SECTION 2

Ensure the patient receives a full dose of medication every time

Patients who use their inhalers on an as-needed basis may improve compliance through pMDIs that utilize retention valves that do not require frequent re-priming.

Most pMDI valves operate by refilling the metering areas as the valve stem is released after a shot is fired from the unit. If there is an extended period of time between uses, all or part of the formulation may escape the metering area. This is known as loss of prime (LOP) when referring to the propellant and loss of dose (LOD) for the active pharmaceutical ingredient (API). To protect from this, patients are generally advised to fire a priming shot if the inhaler has been left for longer than recommended. This can result in poor patient compliance either through lack of understanding or a desire to save what may be seen as a wasted dose.

While valve designs are under development that capture the dose as the inhaler is fired, eliminating the need for priming, companies can reduce the need to prime in their current products by incorporating existing retention-style valves, such as the 3M™ Retention Valve. This valve retains prime for seven or more days, helping ensure patients get accurate doses of medication even after an extended period of time between inhaler uses, giving physicians more confidence when prescribing the product.

Figure 2-1 3M™ Retention Valve Seven Day Loss of Prime Study

Percentage of Initial Shot Weight

SHOT WEIGHT	Stored Up	Stored Down	Stored Horizontal
227 Formoterol	100.5	100.3	101.2
134a Salbutamol	99.2	99.7	99.7
134a Beclomethasone	100.7	100.5	100.6

* LOP (mean of 5 units) showing percentage of Initial Shot Weight retained after 7 days.

SECTION 3

Maintain a consistent appearance between sample and standard packs

Sampling programs should take into consideration not only the medication, but also the device itself.

Familiarity is a strong driver in instilling confidence, and consequently compliance, in asthma and Chronic Obstructive Pulmonary Disease (COPD) patients. That's why the marketing tactic that most directly effects patient change – sampling – is an important one for pharmaceutical companies. Obviously reducing the number of doses in a sample pack is desirable to both decrease the amount of expensive drug given away free, as well as drive patients to switch to a standard prescribed pack sooner.

THE 3M™ SLEEVED CANISTER

Unlike pill sample packs, though, pMDI samples offer a unique challenge since it is important not to change the size, shape or feel of the inhaler for these packs as this may undermine patient confidence. The use of a low fill canister, such as the 3M™ Sleeved Canister, which houses a smaller medicine chamber within a standard sized canister, enables sampling of both the medication and the pMDI device to help drive preference and maintain confidence while improving profit margins with smaller samples.

SECTION 4

Improve formulation stability and product performance

Formulation stability improves product performance and increases shelf life to help decrease waste and improve profitability.

In pMDIs the API is formulated with a hydrofluoroalkane (HFA) propellant (plus excipients if required) within the container closure system (CCS). Depending on its molecular properties, the API may be formulated as suspension or, through the addition of a co-solvent, a solution. Both routes can lead to interaction between the API and the CCS. For suspension formulations the interaction can cause deposition on the canister wall and exposed surfaces of valve components, which can lead to a reduction in drug content of the formulation. For solution formulations, interactions more commonly cause degradation leading to both reduced drug content and increased impurity levels.

Coatings, like those offered by 3M, can be applied to the canister and valve components to protect the contents from deposition and degradation. This will improve performance and help extend a product's shelf life.

UNTREATED METERING TANK

FLOURINATED ETHYLENE PROPYLENE COATED METERING TANK

SECTION 5

Utilize proven technology in new developments

The use of proven technology can help mitigate risk while building on patient familiarity to help deliver patient and prescriber preference.

Introducing new technology during product development can add additional time and risk to projects, including potential rejection by patients who may be unwilling to gamble on unfamiliar delivery methods. Utilizing proven, patient-friendly technology that has been updated for today's molecules delivers the reassurance that necessary pharmaceutical performance criteria, such as dose delivery, can be accomplished without jeopardizing the product's timeline or chances for technical success.

One example is the 3M™ Retention Valve. This all-metal valve based on the proven Spraymiser™ model (the original retention valve) helps to ensure the valve performs under a wide variety of conditions and patient use regimes. With the addition of a clean Ethylene-Propylene Diene Terpolymer (EPDM) elastomer the valve offers low extractable and leachable levels, low moisture ingression and low levels of elastomer swell while maintaining fundamental performance features such as the ability to be pressure filled and uniformity of delivered dose. The following charts illustrate key performance factors for the 3M™ Retention Valve.

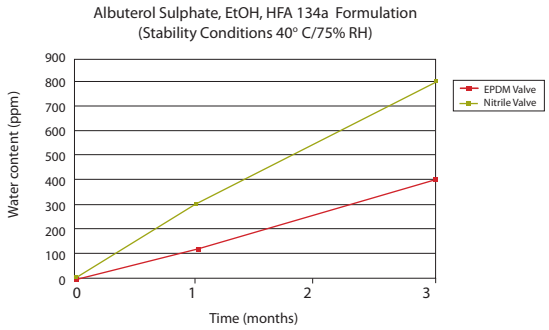


Figure 5-1
Relative Moisture Ingress for 3M valves utilising EPDM and nitrile elastomers

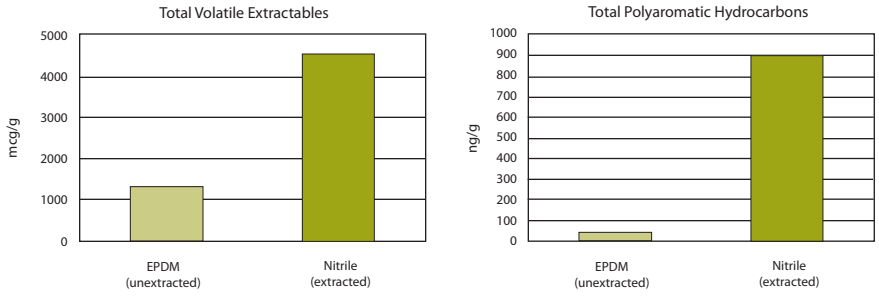


Figure 5-2
Extractables levels for extracted Nitrile elastomer compared with unextracted EPDM elastomer

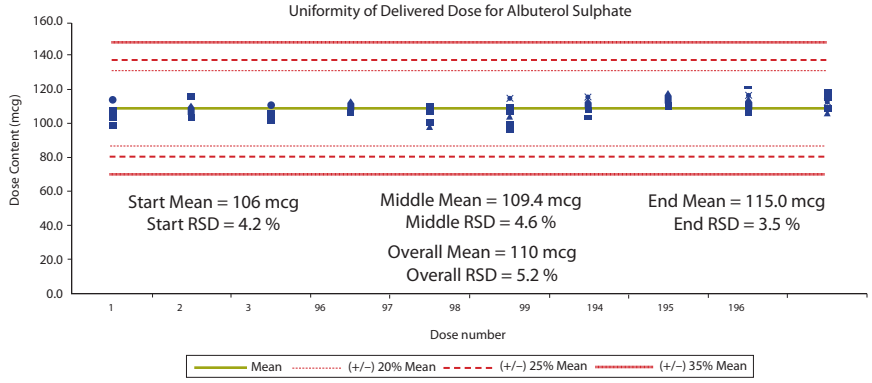


Figure 5-3
Uniformity of Delivered Dose for Albuterol Sulphate, ethanol, HFA134a formulation, 3 months 40° C/75%RH

SECTION 6

Differentiate products in the marketplace

Adding features that improve patient experience can help pharmaceutical companies defend their products against generic substitution.

The continuing escalation in product development costs means pharmaceutical companies are under increasing pressure to find ways to increase revenues from existing products and to stem sales erosion following the launch of generic equivalents. By enhancing products through improvements to delivery technologies and the addition of features to improve performance in the hands of patients, pharmaceutical companies can prolong patent protection, defend their brands against generic substitution and open up opportunities to engage new patients.

THE 3M™ AUTOHALER™

There are a number of technologies in development which may enhance patient experience. The addition of a dose counter to alert patients as to when to replace their inhaler and enable them to more accurately monitor use is one such example (see section 1). Another opportunity is to offer breath-actuated operation. The basic principle of the pMDI requires patients to press and breathe simultaneously. While many patients are able to coordinate these actions adequately to receive an effective dose, some patients find it difficult and may benefit from the use of a breath-activated device, such as the 3M™ Autohaler™. The Autohaler device was developed by 3M to trigger actuation as the patient breathes in, helping ensure patients receive their full dose of medication. During 2008 3M will have produced more than 100 million Autohaler devices, which have been incorporated into products such as Airomir™, Qvar™ and Maxair™.

Other technologies may be incorporated which, while not as obvious to the patient, offer significant improvement in terms of product performance. For example, because most patients do not understand how pMDIs work, they are unaware of the importance of shaking their inhalers correctly or of priming their inhalers after periods of non-use. New valves, such as the 3M™ Face Seal Valve currently under development by 3M, have been designed to address this issue. The 3M Face Seal Valve is a new type of pMDI valve that captures the dose as the inhaler is operated, negating the need for the patient to prime the inhaler before use. Its design not only meets the regulatory expectations for product performance, but is also more robust in real-life patient usage.

Lifecycle management may also offer a route to increased revenue from existing pMDI products. This is especially true of APIs with potential applications in other therapies, such as allergic rhinitis, since expansion of existing pulmonary products into another format, in this case nasal, uses much of the original technology. Focusing changes on the actuator, and utilizing the existing formulation and container closure system data plus experience gained from the original development program, can significantly speed up the development process. Additionally, some aspects, such as certain toxicology and extractables studies (assuming no changes are made to contact materials), may not need to be repeated for the new submission, further speeding the route to product approval. Overall, creating new applications for existing molecules and extending their lifecycles can deliver a substantial return on investment when compared with the full development program required for new drug substances.

SECTION 7

Ensure long-term manufacturability

To be successful, your pharmaceutical product must be readily available and consistently manufactured over the course of its lifecycle.

Having the right product at the right time is only half the story. Companies must be able to maintain a product's positive momentum throughout its lifecycle to help ensure success. That means that when choosing a manufacturing partner, companies must consider not only the cost of individual components but also the consistency and robustness of the manufacturing processes if manufacturability is to be maintained over the product lifetime and batch release costs are to be kept to a minimum.

Additionally, a manufacturing partner must have the flexibility to quickly scale-up production as needed from development through commercialization to keep the product development pipeline ahead of the competition while still meeting the requirements of regulators and customers with cGMP compliant practices..

As a leading drug delivery developer, 3M has extensive expertise in the field of manufacturing. From pilot to full-scale production, use of state-of-the-art processes enables cost-effective, on-time delivery with the highest level of customization and quality. However, it is the 3M team's experience and expertise that separates 3M from the competition. With a long track record of innovative problem solving and successful New Drug Applications (NDAs), 3M offers customers complete support and documentation for the development of new molecules as well as delivery optimization and enhancement for already established products.

Bring the patient voice to product development

Putting patients at the heart of development benefits pharmaceutical companies through improved compliance and increased patient and prescriber preference.

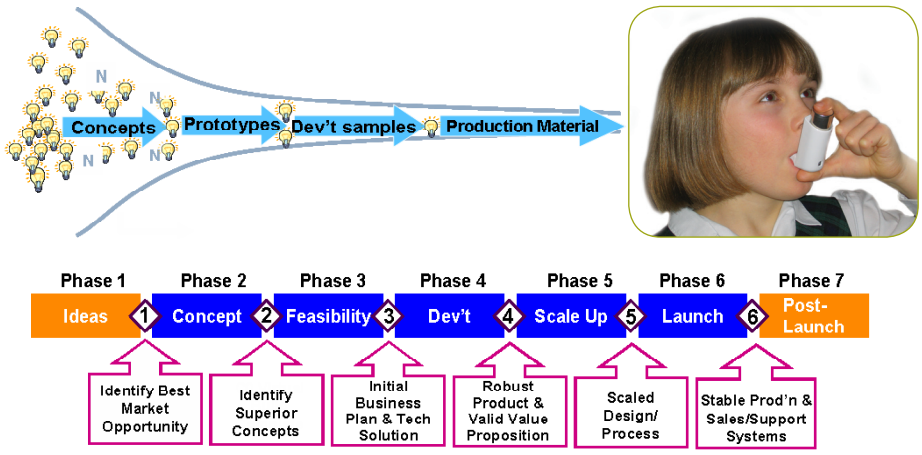
Bringing new products to market is a slow process. As developments progress it is important to consider patient needs as well as determine probability of acceptance of new drug delivery options. Putting patients at the heart of drug delivery product design can accelerate the process of bringing products to market in a patient-friendly way and drive patient and prescriber preference. Improvements that enhance the patient experience can increase patient preference for an individual product and increase prescribers' confidence that the patients can, and will, use the device correctly. Patient-friendly enhancements not only differentiate the product from competitors but also drive loyalty, helping to protect the product from substitution.

From the beginning, when the first pMDI was inspired by a young patient who was struggling with a glass bulb nebulizer, 3M has developed products and technologies with a patient focus. Today 3M continues to invest in global research in order to understand how patients interact with inhalers.

It is ideal to have several stages of patient research. Exploratory research looking at broad customer needs and gaps in technologies should be conducted on a regular basis to initiate development opportunities. Once early concepts have been developed they can be tested with patients, allowing revisions to be made according to the responses obtained. Ideally the final product solution should be validated with patients before large financial commitments are made to scale-up and commercialize products. Finally, no system would be complete without ensuring that learning gained throughout development and launch is fed back into new product ideas and concepts.

With this in mind, a New Product Introduction system (Figure 8-1) was specially designed for 3M to include in-depth customer focus throughout the development process alongside the more traditional technical, manufacturing and business deliverables.

Figure 8-1
New Product Introduction System (Product development and commercialization)



This level of experience is critical when conducting patient research to ensure research design is robust. To deliver true value, studies must be carefully thought out if findings are to be representative of actual uptake following launch. The consequences of not doing so can be commercially disastrous. It has been suggested that this may have contributed to the lack of uptake of Exubera™. Patients willing to enter clinical studies for non-injection delivery of insulin may have been a patient group more predisposed to learning new techniques for delivery than the general patient population. It is critical to consider such eventualities when planning research.

Each program of patient research conducted enhances the overall understanding of patient lifestyles, inhaler interaction and general preferences and, as such, it is important to ensure learning from one project can be fed back along the development process into others.

Through this methodology 3M was able to use previous research to understand the primary patient needs for the inclusion of a dose tracker in the design of their Integrated Dose by Dose Counter. During concept design, 3M's designers were able to utilize previous research to focus on the following criteria indicated by patients as the most important:

- *Displays individual count*
- *Retains inhaler look and feel*
- *Accurate*
- *Fits in hand*
- *Robust design stands up to real-life use*

These features were validated during patient research, which compared this configuration to other approaches. By putting patients at the center of development, customers can be assured that 3M products and technologies will be well-received by patients and prescribers alike.

SECTION 9

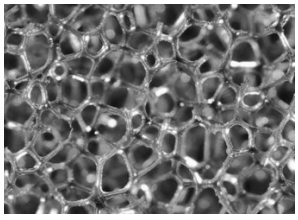
Utilize new technology to enable the delivery of “difficult” formulations

New anti-flocculating components can negate the need to reformulate or abandon a formulation when dosing irregularities caused by rapid flocculation occur.

Most current pMDI formulations are comprised of suspensions of one or more micronized active compounds in a hydrofluoroalkane (HFA) based propellant system. Such formulations have a tendency of rapid flocculation followed by either creaming or sedimentation, depending on the relative density of the solids to the propellant mixture. This can lead to inconsistent dosing if the formulation is not re-dispersed sufficiently before the next dose is taken.

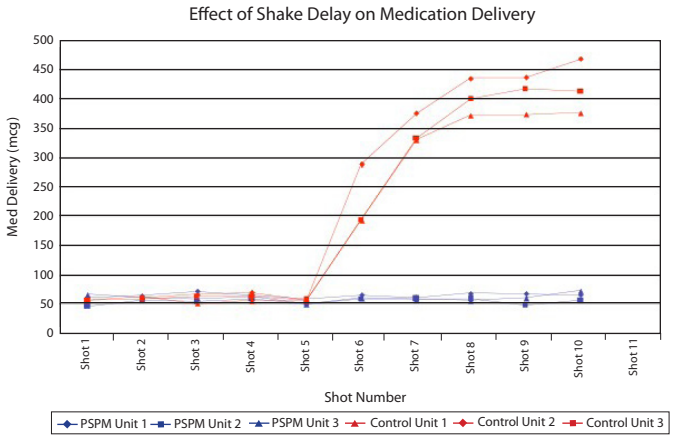
To overcome this problem 3M Drug Delivery Systems has developed a unique semi-permeable system component to act in synergy with a flocculating suspension formulation. This particulate semi-permeable matrix (PSPM) technology has been shown to improve the dosing uniformity of these rapidly flocculating formulations and therefore can negate the need to reformulate or even abandon a formulation when dosing irregularities caused by rapid flocculation are encountered. Medication delivery results for a zero ethanol HFA 134 albuterol formulation tested can be see in figure 9-1.

In this study units containing the PSPM technology were tested against control units. Units were primed and then shots 1 to 10 were collected and analysed for medication delivery. Shots 1 to 4 were fired using a standard shake technique and shots 5 to 10 were fired following a 30 second delay after shaking. Results clearly show the PSPM technology delivers a consistent dose even after the rapidly flocculating formulation has sedimented following shake delay. The new technology was recognized as one of the most innovative ideas presented at the Drug Delivery to the Lungs conference in Edinburgh in 2006 and was awarded the annual poster prize.



DETAIL OF RETICULATED FOAM

Figure 9-1
Effect of 3M PSPM Technology on Medication Delivery (ex Actuator) following Shake Delay



SECTION 10

Reduce product development risk

By reducing risk, companies can optimize product development pipelines to bring better products to market, faster.

Out of all the drug candidates selected for development in the pharmaceutical industry, only a few make it to clinical trials. Fewer still go on to become successful, profitable products. To shift the odds in your favor, companies should seek out and utilize experienced partners, proven processes and increasingly advanced technologies to help reduce risk.

Figure 10-1
Kelly, John M.D. The Drug Discovery, Development and Approval Process. www.phrma.org.

	Discovery/ Preclinical Testing	Clinical Trials: Phase I	Clinical Trials: Phase II	Clinical Trials: Phase III			Phase IV
Years	6.5	1.5	2	3.5	1.5	15 total	Additional post-marketing testing required by FDA
Test Population	Lab and animal studies	20 to 100 healthy volunteers	100 to 500 patient volunteers	1,000 to 5,000 patient volunteers	Review process/ approval		
Purpose	Assess safety, biological activity and formulations	Determine safety and dosage	Evaluate effectiveness, look for side effects	Confirm effectiveness, monitor adverse reactions from long-term use			
Success Rate	5,000 compounds evaluated	5 enter trials			1 approved		

File IND at FDA

File NDA at FDA

3M Drug Delivery Systems offer more than 50 years of experience and proven success in inhalation technologies. From unique formulations and mechanical challenges to global regulatory support, 3M can draw on its vast community of experts as well as leading-edge technologies to reduce risk, solve issues and deliver a customized solution. It's part of an ongoing culture of innovation that's created a lot of firsts, including the first pressurized Metered-Dose Inhaler (pMDI), the first non-CFC pMDI, and the first single cycle review for a pMDI in the USA.

From pilot to full scale, 3M can provide a competitive advantage in reliability and flexibility with a full range of cGMP compliant development and manufacturing capabilities that can be customized to your specific needs. With state-of-the-art facilities currently producing more than 60 million pMDIs for worldwide distribution each year, 3M has the capacity to meet your needs now and in the future. Lean Six Sigma methodology ensures quality and consistency throughout the life of your product.

3M Drug Delivery Systems

INHALATION SYSTEMS & COMPONENTS

When you need drug delivery results, experience matters.

3M Drug Delivery Systems offers more than 50 years of experience and proven success in technology, product development and manufacturing, coupled with our global regulatory expertise. We can offer a partnership that ensures a smooth process from start to finish and help you bring your products to market more quickly. Working with us, you get the speed to market that's critical to the success of your new application.

ENABLING YOUR SUCCESS.

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